

National Aeronautics and Space Administration



# GeneLab: “Omics” Data Systems for Spaceflight and Simulated Spaceflight Environment

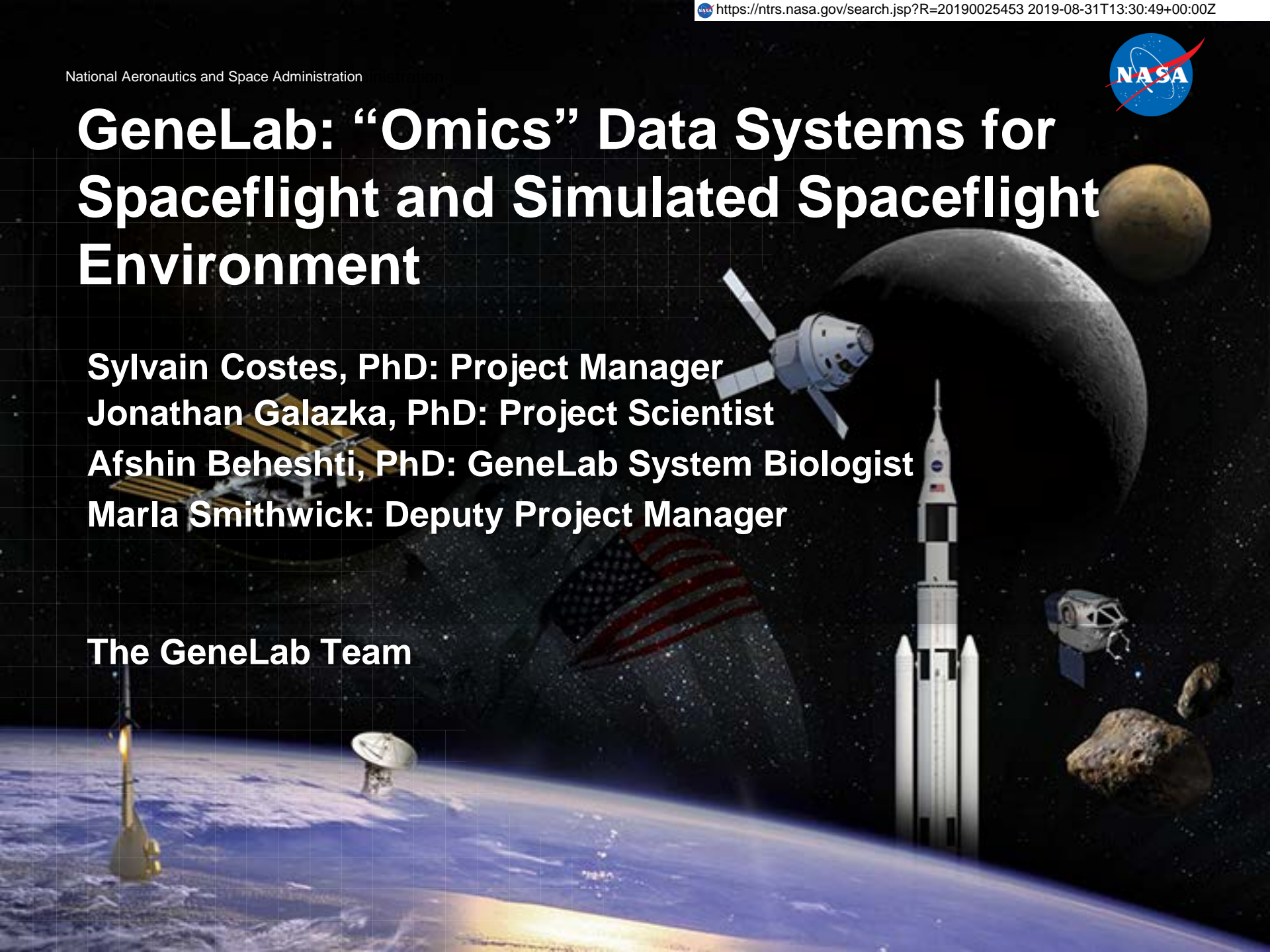
**Sylvain Costes, PhD: Project Manager**

**Jonathan Galazka, PhD: Project Scientist**

**Afshin Beheshti, PhD: GeneLab System Biologist**

**Marla Smithwick: Deputy Project Manager**

**The GeneLab Team**



# Challenges of Spaceflight



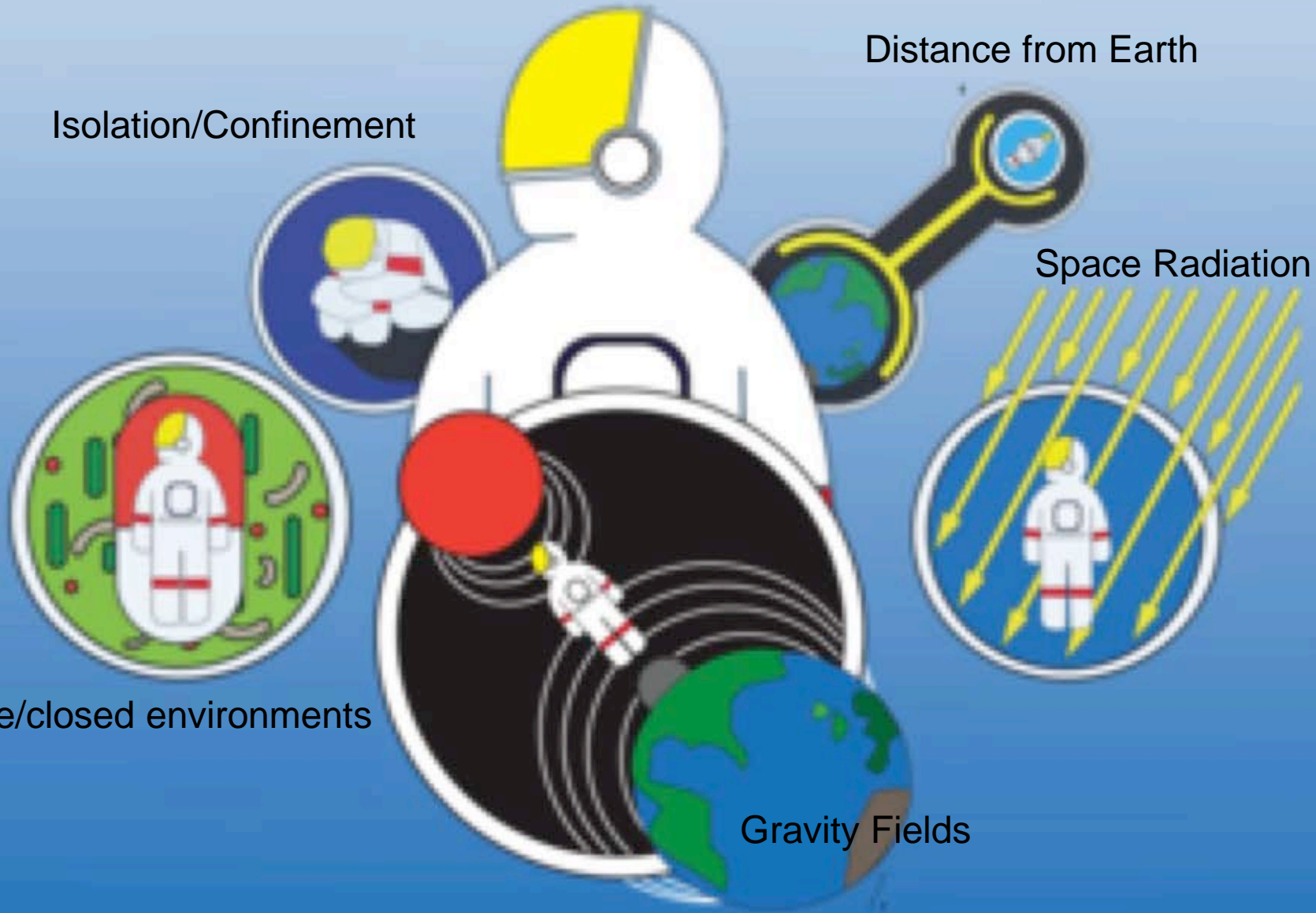
Isolation/Confinement

Distance from Earth

Space Radiation

Hostile/closed environments

Gravity Fields

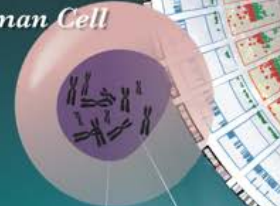




# OMICS

*A Circular  
Genome  
Visualization*

*Human Cell*



*Telomere*

*Chromosome*

*Chromatin*

*Telomere*

*Metabolites*

*Proteins*

*RNA*

*Telomere*

*Methyl  
Groups*

*DNA*

**A Journey to See More  
Than Ever Before**



## Recapturing a Future for Space Exploration

Life and Physical Sciences Research for a New Era

NATIONAL RESEARCH COUNCIL  
OF THE NATIONAL ACADEMIES

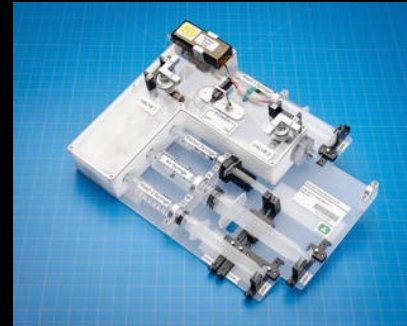
*“...**genomics, transcriptomics, proteomics, and metabolomics** offer an immense opportunity to understand the effects of spaceflight on biological systems...”*

*“...Such techniques generate considerable amounts of **data that can be mined and analyzed** for information by multiple researchers...”*



# Acquisition in Space is Now a Reality

This is truly an exciting time for cellular and molecular biology, omics and biomedicine research on ISS with these amazing additions to the suite of ISS Laboratory capabilities.



**Sample Preparation Module**

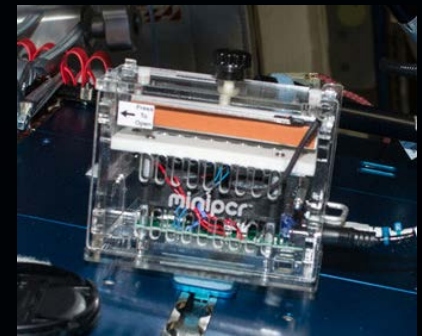


**Oxford Nanopore MinION Gene Sequencer**

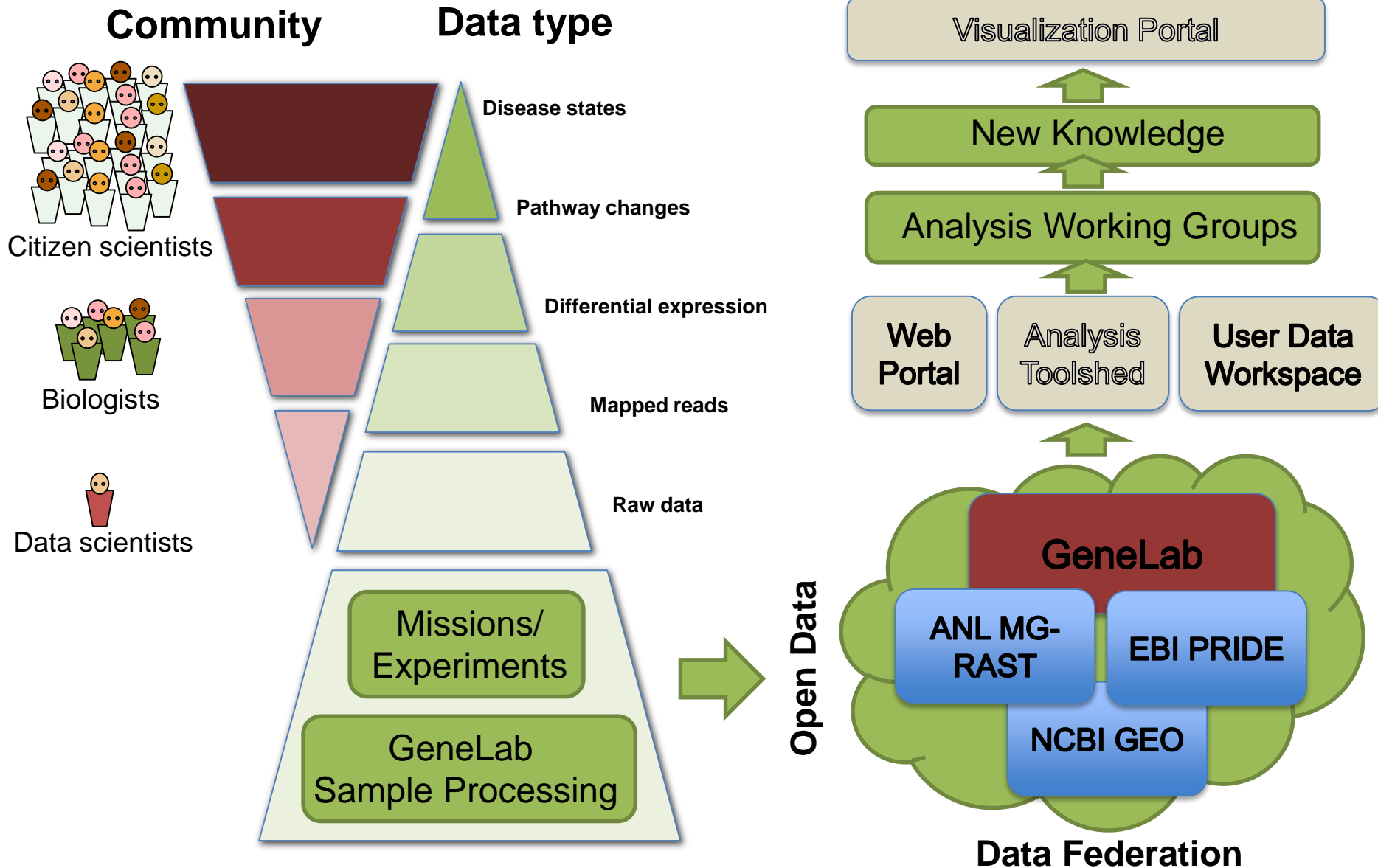
**Cepheid Smart Cycler qRT-PCR**



Reaction tube containing lyophilized chemical assay bead (proprietary)



**Mini-PCR**





## Data federation/integration with heterogeneous bioinformatics external databases (GEO, PRIDE, MG-RAST)

### Federated Search

mouse myostatin x Q

☐ All ☒ GeneLab ☒ NIH GEO ☐ EBI PRIDE ☐ ANL MG-RAST

Search results for: **mouse myostatin** using filter(s):

Sort by Relevance 25

**Myostatin inactivation effects on myogenesis in vitro and in vivo**  
<http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE28986>



Key words: dystrophin, mdx mouse, Duchenne, fibrosis, dystrophy ABSTRACT Stm (MDSC) into myogenic, as opposed to lipofibrogenic, lineages is a promising therapeutic counteracting myostatin, a negative regulator of muscle mass and a pro-fibrotic fibrogenic capacity of MDSC from wild...

Organism: Mus musculus Accession: GSE28986 PI/Contact: Robert Gelfand Release

**The transcriptomic signature of myostatin inhibitory influence on the differentiation of skeletal muscle**  
<http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE59674>



GDF8 (myostatin) is a unique cytokine strongly affecting the skeletal muscle phenotype. Molecular mechanism of myostatin influence on the differentiation of mouse C2C12 myoblasts. Treatment with exogenous GDF8 strongly affected the growth and development, proliferation and differentiation...

Organism: Mus musculus Accession: GSE59674 PI/Contact: Zofia Wikik Release

**Development of gene expression signature for defining the cell potency of muscle progenitor cells**  
<http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE39765>



In order to determine the cell potency, by identification of genes responsible for pluripotency, we isolated from five week old male wild type (WT), C57BL/6J and another hypertrophied microarray analysis and compared this gene expression to that of a standard mouse and Mstn null mice using an established protocol...

Organism: Mus musculus Accession: GSE39765 PI/Contact: Bipasha Bose Release

**Rodent Research-3-CASIS: Mouse liver transcriptomic proteomic and epigenetic data**  
<https://genelab-data.ndc.nasa.gov/genelab/accession/GLDS-137>



The Rodent Research-3 (RR-3) mission was designed to study the effectiveness of occurs during spaceflight. Myostatin is a protein secreted by myoblasts that inhibits myoblast proliferation and causes increases in muscle mass. The RR-3 experiment was sponsored by NASA to study the effects of spaceflight on muscle mass and function. Advancement of Science in Space and associated research...

Organism: Mus musculus Factor: Microgravity Treatment Assay Type: transcription profile Accession: GLDS-137

**GeneLab**  
Open Science for Exploration

### Search Filters for GeneLab

Home Repository Data Data Mining Tools Submit Data Help Workspace

mouse x Q

☐ All ☒ GeneLab ☐ NIH GEO ☐ EBI PRIDE ☐ ANL MG-RAST

#### Search Filters (GeneLab Only)

Project Type	Factors	Organisms	Assay Type
<input checked="" type="checkbox"/> Ground <input type="checkbox"/> Spaceflight	<input checked="" type="checkbox"/> Age <input type="checkbox"/> Anatomical Structure <input type="checkbox"/> Antibiotic concentration <input type="checkbox"/> Atmospheric Pressure <input type="checkbox"/> Bed Rest <input type="checkbox"/> Bleomycin Treatment <input checked="" type="checkbox"/> cage <input type="checkbox"/> Age play <input type="checkbox"/> Epidemic <input type="checkbox"/> Accumulation <input type="checkbox"/> Decreases <input type="checkbox"/> cell culture <input type="checkbox"/> clinical treatment	<input checked="" type="checkbox"/> Mus musculus <input type="checkbox"/> Mycobacterium mar... <input type="checkbox"/> Oryzias latipes <input type="checkbox"/> Pantoea conspicua <input type="checkbox"/> Pseudomonas aeru... <input type="checkbox"/> Rattus norvegicus <input type="checkbox"/> Rhodospirillum rubr... <input type="checkbox"/> Saccharomyces cer... <input type="checkbox"/> Staphylococcus <input type="checkbox"/> Staphylococcus aureus	<input type="checkbox"/> deletion pool profiling <input type="checkbox"/> DNA methylation profiling <input type="checkbox"/> environmental gene survey <input type="checkbox"/> genome sequencing <input type="checkbox"/> metabolite profiling <input type="checkbox"/> protein expression profiling <input type="checkbox"/> RNA methylation profiling <input type="checkbox"/> transcription profiling

Factor Name = Age' OR 'Study Factor Name = cage'

Total Search Results Found: 3

1

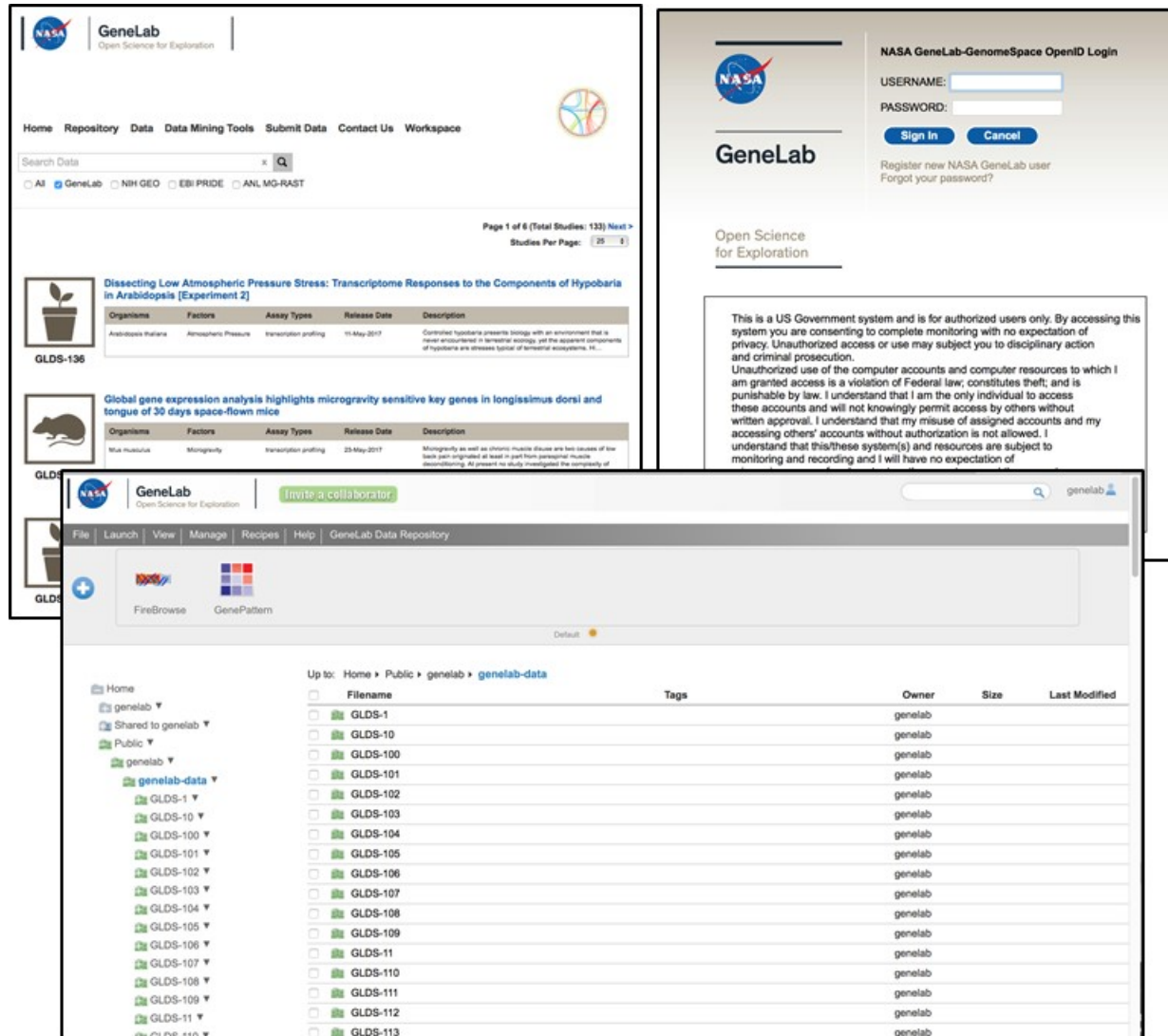
**Age and Space Irradiation**  
<https://genelab-app-1-st...>

Age play  
Epidemic  
Accumulation  
Decreases  
cell culture  
clinical treatment  
Organism: Mus musculus

**carcinogenesis Risk**  
modeling the carcinogenesis process or estimating cancer risks. Cancer incidence increases with age. This effect is commonly attributed to a lifetime of middle-age the incidence begins to decelerate and for many tumor sites it actually decreases with age.

Accession: GLDS-88 PI/Contact: Christine Afshin Edward L...

## User Account Mgmt., Access Controls (e.g., Private, Shared, Public Folders)



The image displays three overlapping screenshots of the GeneLab interface, illustrating user account management and access controls.

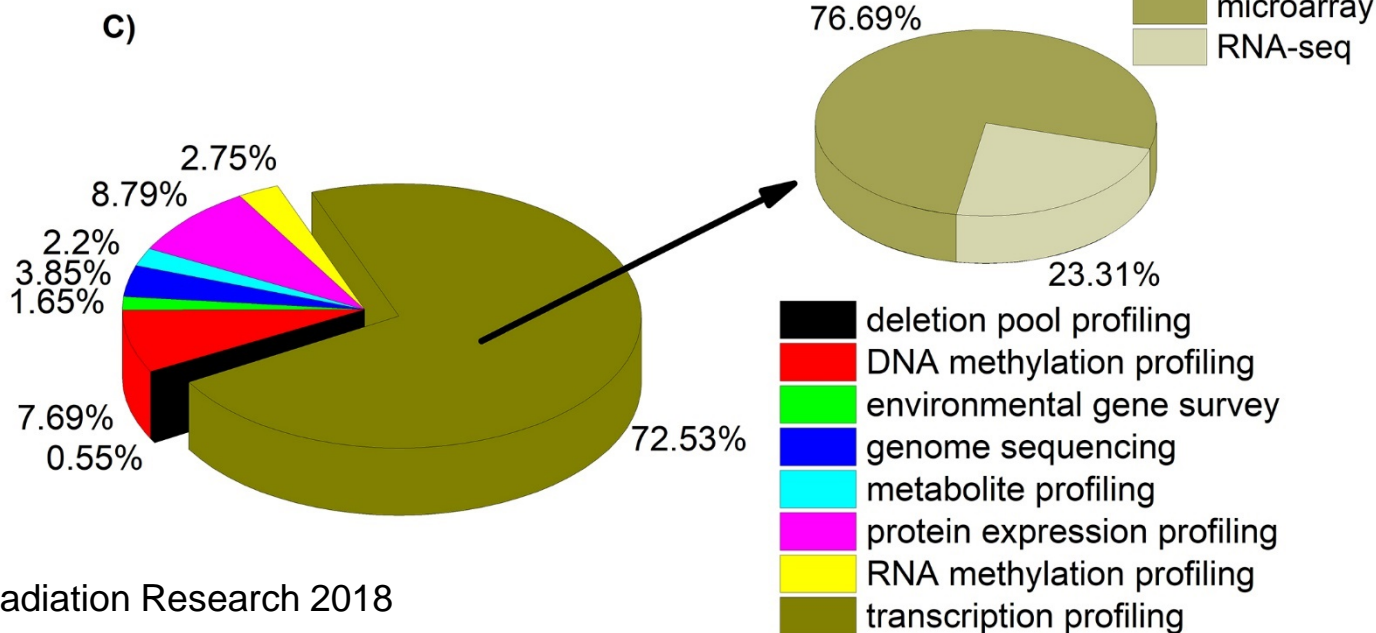
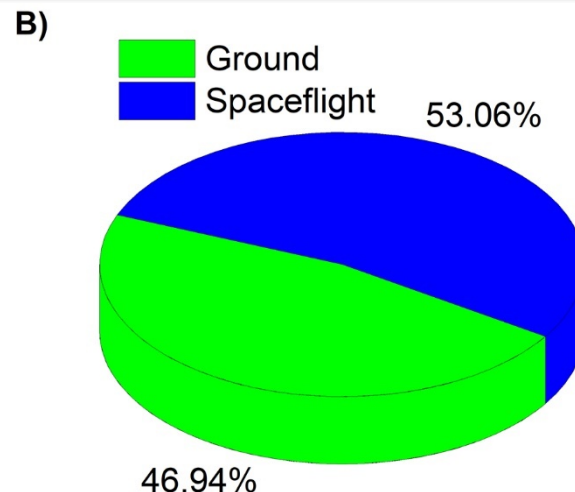
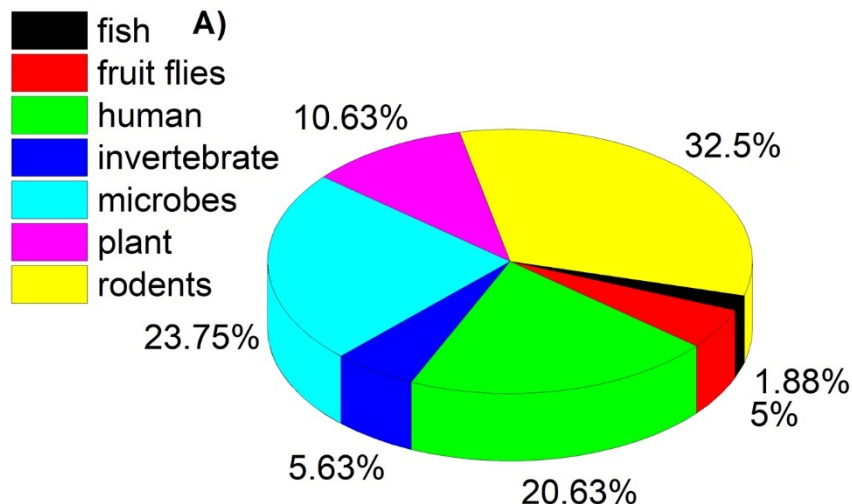
**Top Left Screenshot:** Shows the main GeneLab workspace. The header includes the NASA logo and "GeneLab Open Science for Exploration". The navigation bar contains links: Home, Repository, Data, Data Mining Tools, Submit Data, Contact Us, and Workspace. A search bar is present with a dropdown menu showing filters: All, GeneLab (selected), NIH GEO, EBI PRIDE, and ANL MG-RAST. Below the search bar, a list of studies is displayed. The first study is "Dissecting Low Atmospheric Pressure Stress: Transcriptome Responses to the Components of Hypobaria in Arabidopsis [Experiment 2]" (GLDS-136). The second study is "Global gene expression analysis highlights microgravity sensitive key genes in longissimus dorsi and tongue of 30 days space-flown mice" (GLDS-137).

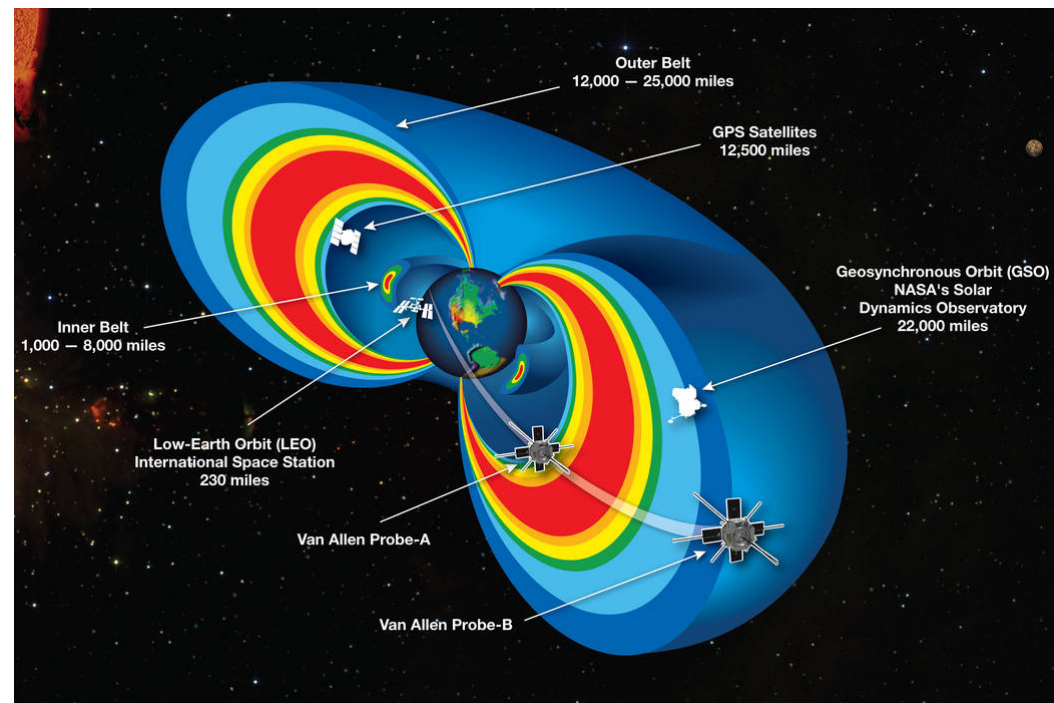
**Top Right Screenshot:** Shows the login page. The header includes the NASA logo and "GeneLab Open Science for Exploration". The main heading is "NASA GeneLab-GenomeSpace OpenID Login". There are input fields for USERNAME and PASSWORD, and buttons for "Sign In" and "Cancel". Below the login fields, there are links for "Register new NASA GeneLab user" and "Forgot your password?". A disclaimer box is visible at the bottom, stating: "This is a US Government system and is for authorized users only. By accessing this system you are consenting to complete monitoring with no expectation of privacy. Unauthorized access or use may subject you to disciplinary action and criminal prosecution. Unauthorized use of the computer accounts and computer resources to which I am granted access is a violation of Federal law, constitutes theft, and is punishable by law. I understand that I am the only individual to access these accounts and will not knowingly permit access by others without written approval. I understand that my misuse of assigned accounts and my accessing others' accounts without authorization is not allowed. I understand that this/these system(s) and resources are subject to monitoring and recording and I will have no expectation of..."

**Bottom Screenshot:** Shows a file browser view. The header includes the NASA logo and "GeneLab Open Science for Exploration". The main heading is "GeneLab Data Repository". The navigation bar contains links: File, Launch, View, Manage, Recipes, Help, and GeneLab Data Repository. Below the navigation bar, there are buttons for "FireBrowse" and "GenePattern". The main content area shows a tree view of folders and files. The tree view includes "Home", "genelab", "Shared to genelab", "Public", and "genelab-data". The "genelab-data" folder is expanded, showing a list of files. The list of files includes "GLDS-1", "GLDS-10", "GLDS-100", "GLDS-101", "GLDS-102", "GLDS-103", "GLDS-104", "GLDS-105", "GLDS-106", "GLDS-107", "GLDS-108", "GLDS-109", "GLDS-11", "GLDS-110", "GLDS-111", "GLDS-112", and "GLDS-113". The table below the tree view shows the details of the files, including Filename, Tags, Owner, Size, and Last Modified.

Filename	Tags	Owner	Size	Last Modified
GLDS-1		genelab		
GLDS-10		genelab		
GLDS-100		genelab		
GLDS-101		genelab		
GLDS-102		genelab		
GLDS-103		genelab		
GLDS-104		genelab		
GLDS-105		genelab		
GLDS-106		genelab		
GLDS-107		genelab		
GLDS-108		genelab		
GLDS-109		genelab		
GLDS-11		genelab		
GLDS-110		genelab		
GLDS-111		genelab		
GLDS-112		genelab		
GLDS-113		genelab		





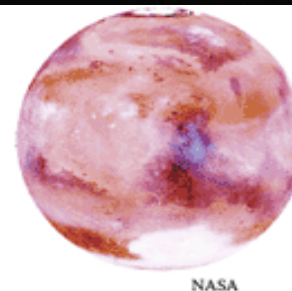


	MILLIREM:
CHEST X-RAY	8 to 50
AVG. YEARLY RADON DOSE	200
U.S. AVG. YEARLY DOSE	350
PET SCAN	1,000
1 YEAR IN KERALA, INDIA	1,300
U.S. NUCLEAR WORKER LIMIT PER YEAR	5,000
APOLLO 14 (9 DAYS)	1,140
SHUTTLE 41-C (18 DAYS)	5,600
SKYLAB 4 (84 DAYS)	17,800
<b>MARS MISSION TOTAL</b>	<b>130,000</b>

## 2½ Years, 2,600 X-Rays

Americans on average absorb the radiation equivalent of at least 7 chest X-rays each year.

Space missions, outside of Earth's protective atmosphere and magnetic field, expose astronauts to many times more.



NASA

TRIP TO AND FROM MARS (1 YEAR): 80,000

ON MARS (1.5 YEARS): 30,000

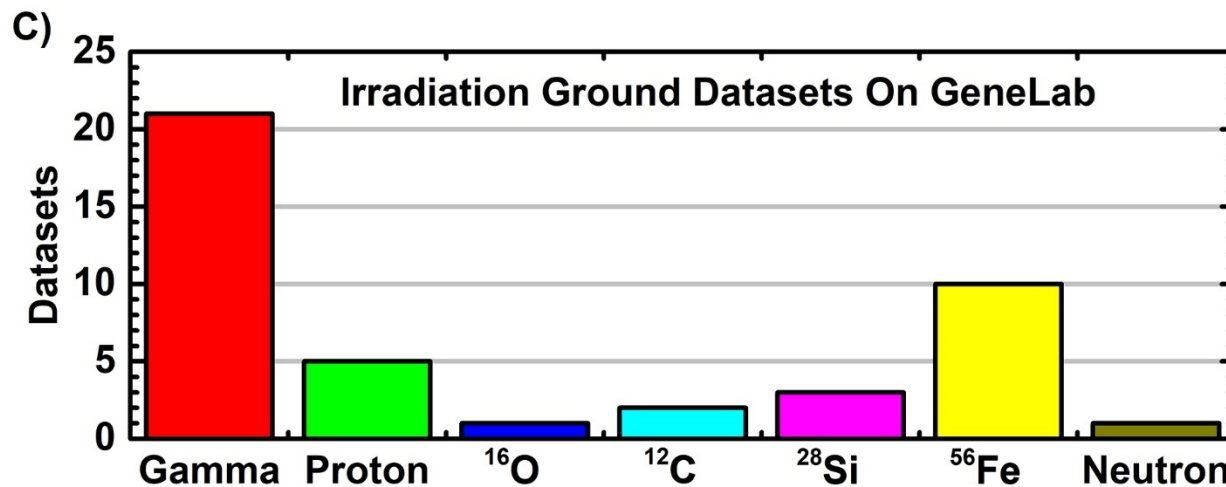
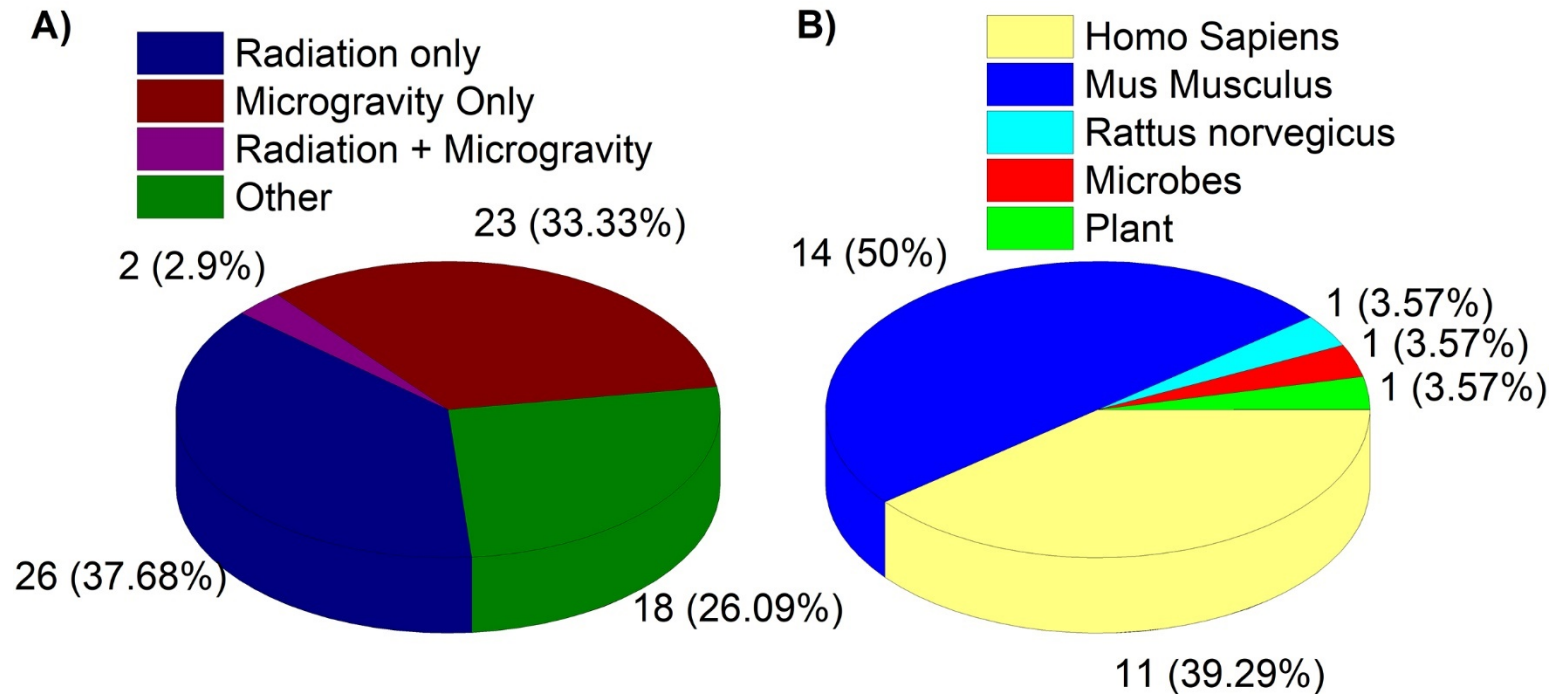
FROM SOLAR FLARE: 20,000





**CAUTION**  
LASER RADIATION  
DO NOT STARE INTO BEAM  
CLASS 3 DIODE LASER(S)  
630-690 nm (RED)  
= 5 mW CONTINUOUS

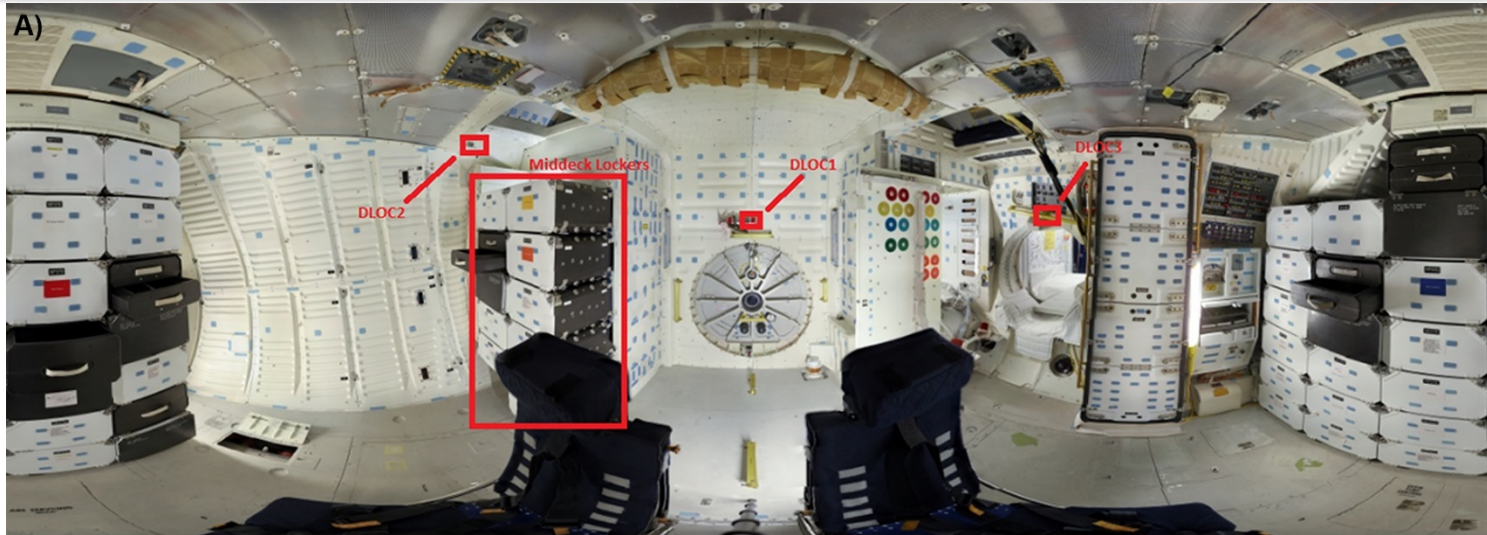
# 69 Ground Data Sets: Radiation and simulated microgravity



Beheshti et al.,  
Radiation Research  
2018

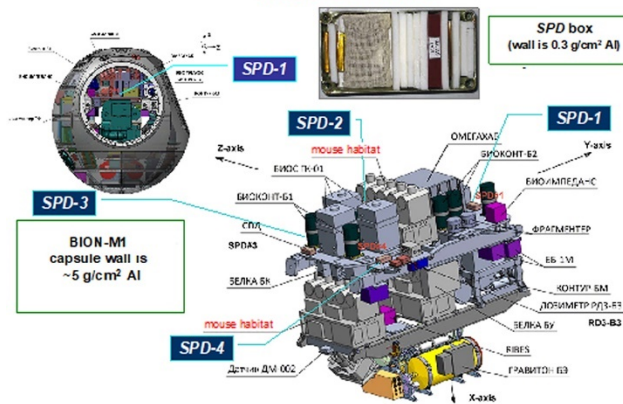


# Radiation Dosimetry for STS samples (ISS to follow)

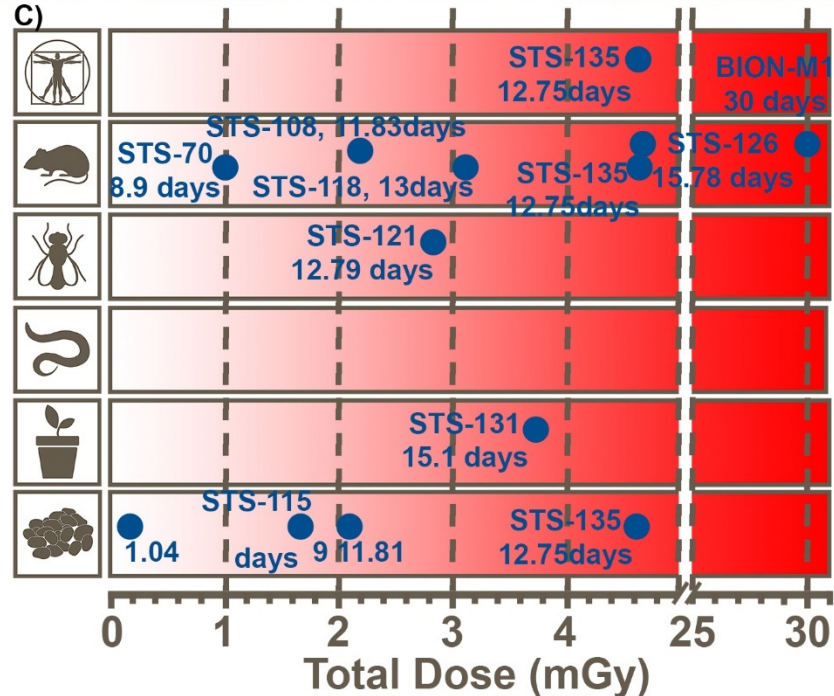


B)

Locations of Radiation Detectors and Animal Holders inside BION-M1



C)



## **Barriers to reproducible analysis of omics data:**

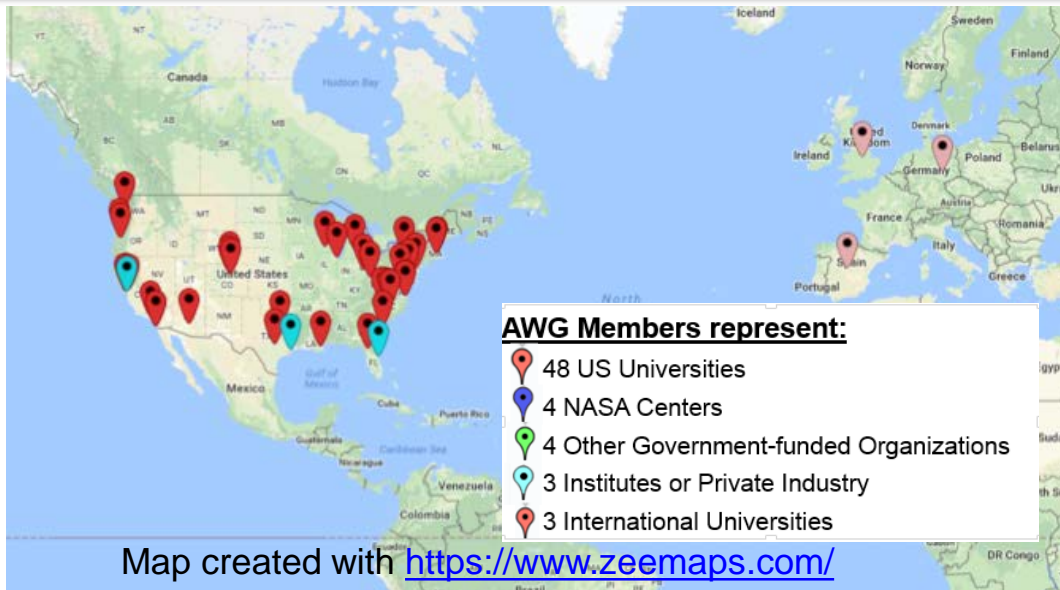
1. Large files are difficult to move around and process
2. Workflows vary from user to user and details are sometimes poorly documented

## **Galaxy platform:**

1. Open source, extensible platform for cloud based analysis of omics data
2. Allows any command line tool or script to be run and chained together into workflows
3. Workflows can published, shared and downloaded



Afgan et al. The Galaxy platform for accessible, reproducible and collaborative biomedical analyses: 2016 update. Nucleic Acids Research (2016)



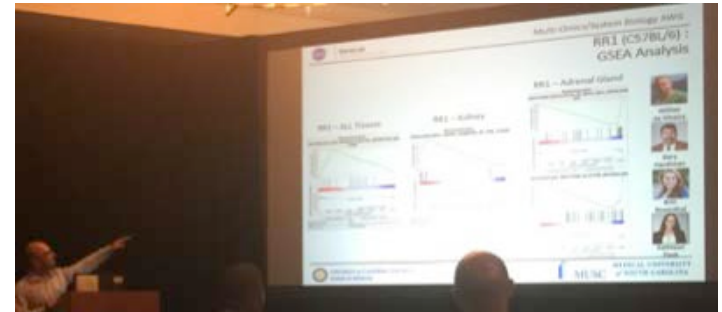
**Total AWG Members: 114**

**AWG Members Per Group:**

Animal	47
Multi-Omics/System Biology	33
Plants	24
Microbes	21

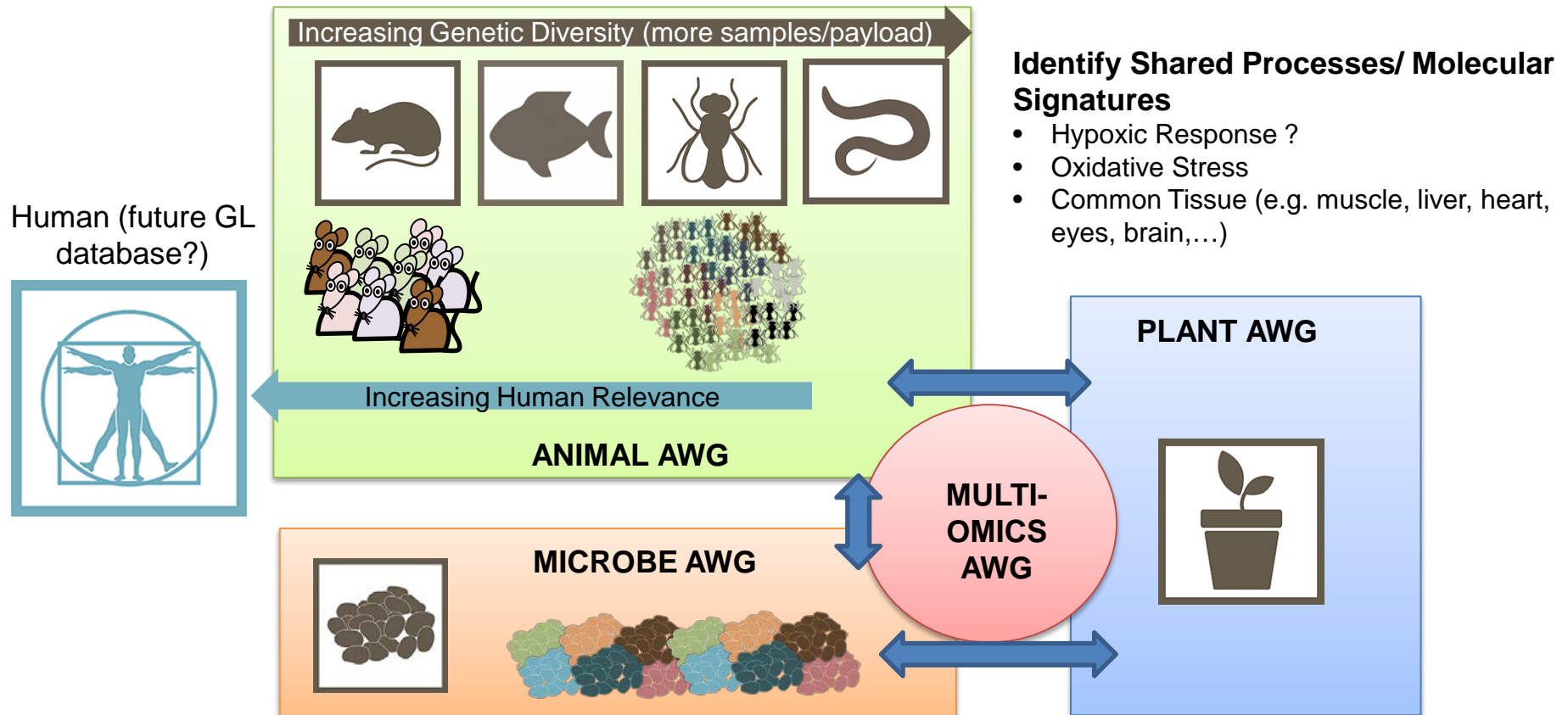
*\*Some members are in multiple groups*

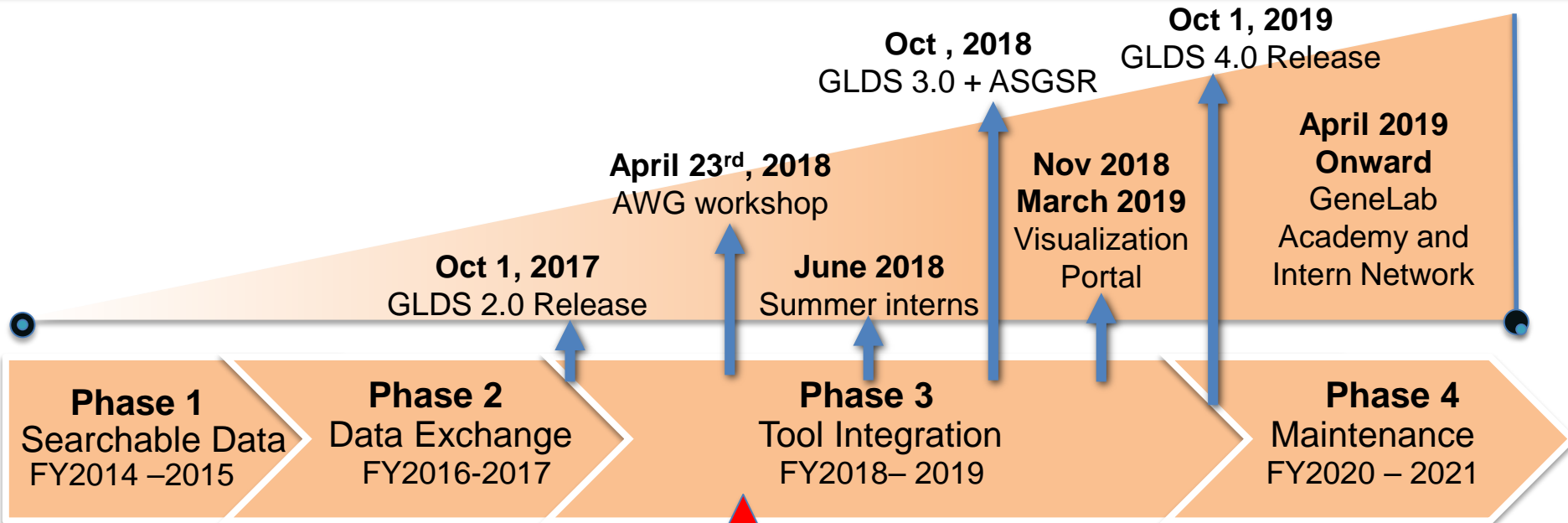
- **Monthly meetings + “Homework”**
- **One Annual Workshop (April)**
- **Summer internship (8 – 10 students for 10 weeks)**
- **Deliverables:**
  - Consensus pipelines for primary analysis of data (Microarray, RNASeq, Bisulfite sequencing, Proteomics, 16S metagenomics, Whole genome metagenomics)
  - Recommendations for visualization of data





# Guiding principles to look at GeneLab data



**Data System**

- ✓ Public Website
- ✓ Searchable Data Repository
- ✓ Top Level Requirements
- ✓ New Data and Legacy Data

**Data System**

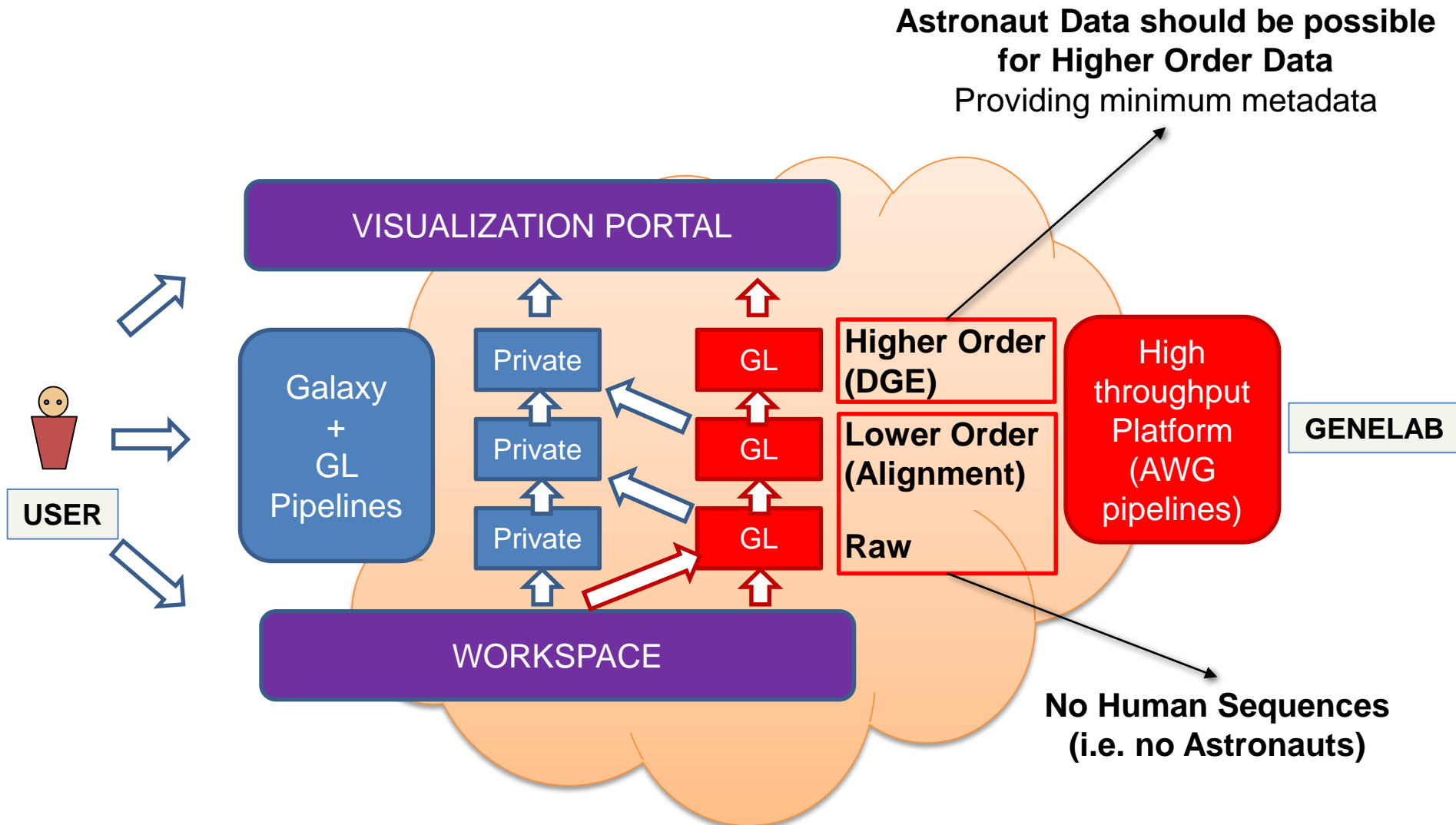
- ✓ Link to Public Databases via Data Federation
- ✓ Integrated Search (e.g., data mashup)

**Data System**

- Integrated Platform across model organisms
- Build Community via AWG
- Provide access to biocomputational tools for omics analysis
- Provide collaboration framework and tools

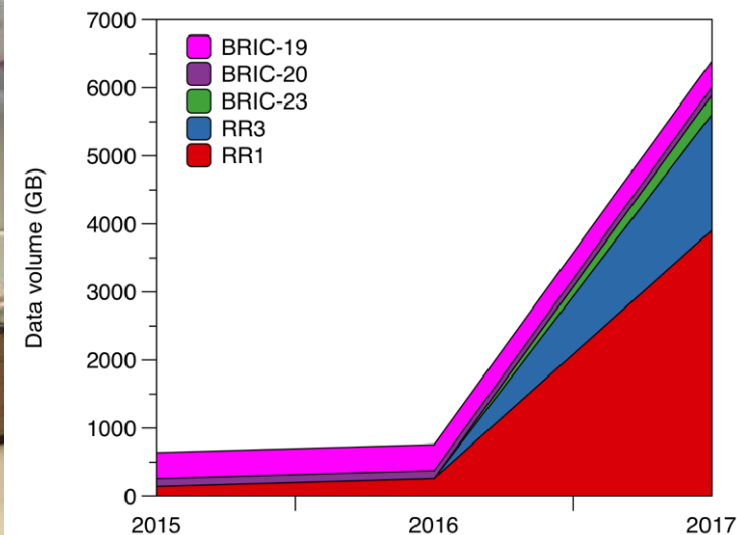
**Open Source Maintenance**

- User community becomes primary provider of new tools/knowledge
- Maintain integrity of data, and data system





- Expertise:
  - DNA/RNA/protein extraction
  - Animal work
  - In-house Sequencing (including Library Prep)
- Develop standards for sample processing (species dependent)
- Responsible for ~50% of GeneLab data by volume – NCI TCGA model: keeping data as consistent as possible.



- Cage Effects with rodent experiments: Carbon Dioxide as an Environmental Stressor in Spaceflight
- Systems Biology analysis reveals biological spaceflight master regulators
- AWG related work determines novel systemic biological factors causing damage due to spaceflight

# Cage Effects with rodent experiments: Carbon Dioxide as an Environmental Stressor in Spaceflight

Beheshti A, Cekanaviciute E, Smith DJ, Costes SV. Global transcriptomic analysis suggests carbon dioxide as an environmental stressor in spaceflight: A systems biology GeneLab case study. Sci Rep. 2018;8(1):4191. doi: 10.1038/s41598-018-22613-1. PubMed PMID: 29520055; PMCID: PMC5843582.



## A) Cage Types

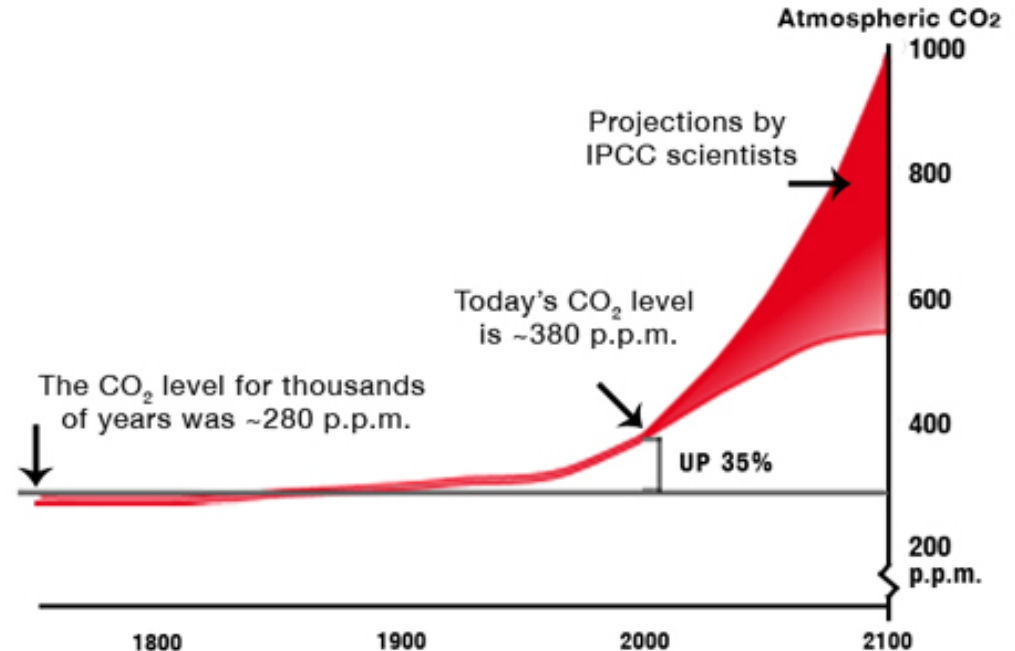


Animal Enclosure Module (AEM)

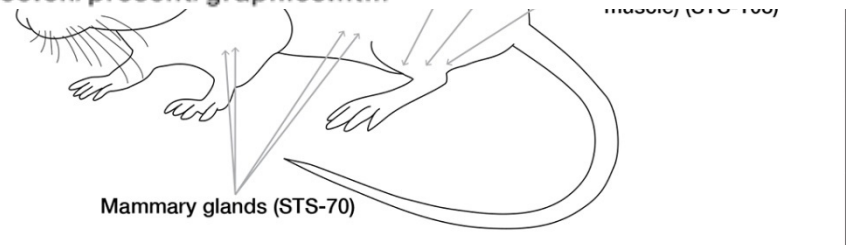
## B)

GeneLab Study	Mission	Species	CO <sub>2</sub> (ppm)	Duration (days)	
GLDS-21	STS-108	mouse	~3000	11.8	
GLDS-111	BF	mouse	~600	30	
GLDS-111	BF	mouse	~600	30	extensor digitorum
GLDS-25	STS-135	mouse	~3000	13	liver
GLDS-63	STS-70	rat	~3000 (est)	9	mammary gland

## Historic and Projected CO<sub>2</sub> Atmospheric Concentrations



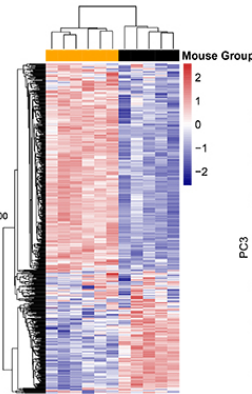
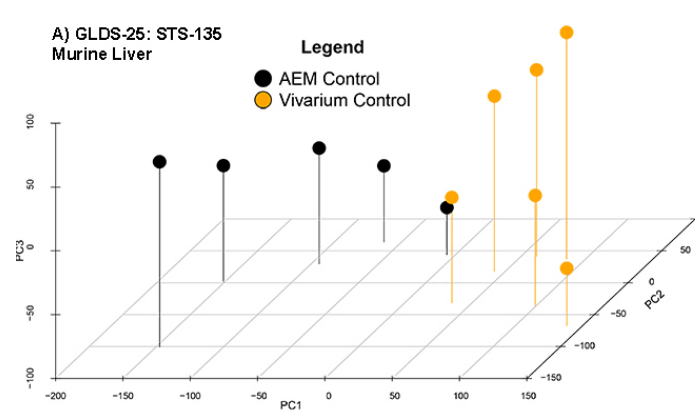
Source: IPCC  
<http://www.ipcc.ch/present/graphics.htm>



3000 ppm

A) GLDS-25: STS-135  
Murine Liver

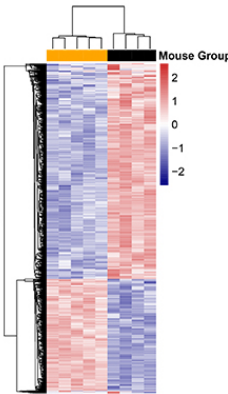
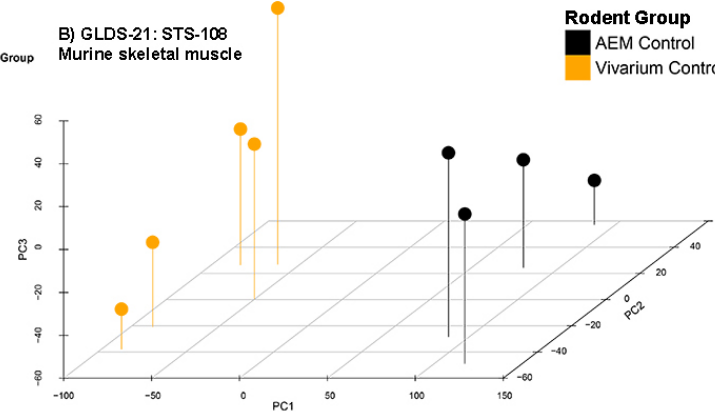
**Legend**  
 ● AEM Control  
 ● Vivarium Control



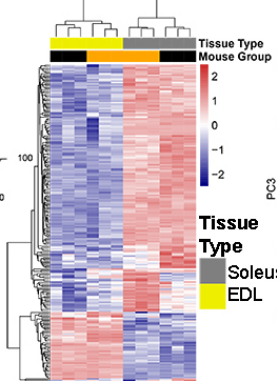
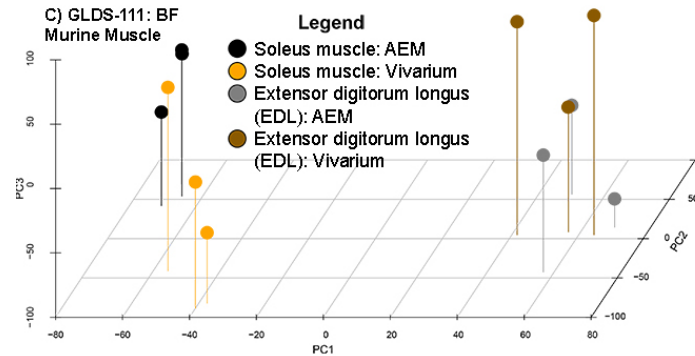
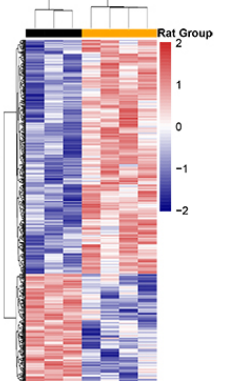
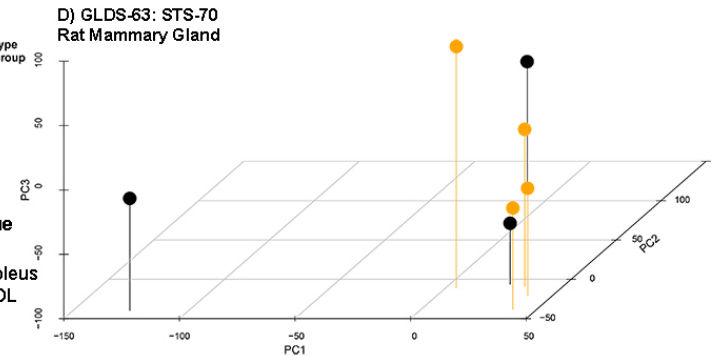
3000 ppm

B) GLDS-21: STS-108  
Murine skeletal muscle

**Rodent Group**  
 ● AEM Control  
 ● Vivarium Control

C) GLDS-111: BF  
Murine Muscle

**Legend**  
 ● Soleus muscle: AEM  
 ● Soleus muscle: Vivarium  
 ● Extensor digitorum longus (EDL): AEM  
 ● Extensor digitorum longus (EDL): Vivarium

D) GLDS-63: STS-70  
Rat Mammary Gland

600 ppm

3000 ppm

AEM = Animal Enclosure Modules (now referred to as Rodent Habitats)  
 Vivarium = normal ground based rodent cages

## A) Venn Diagram of all significant genes

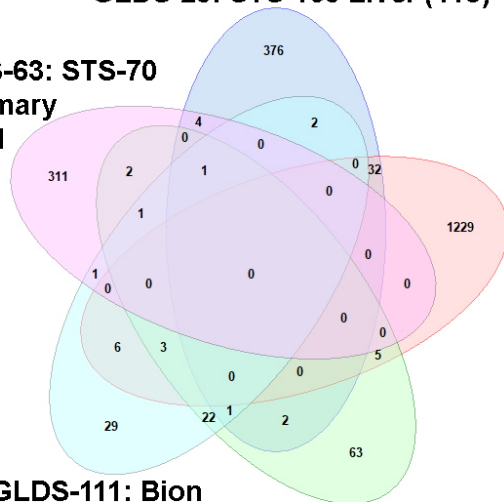
GLDS-25: STS-135 Liver (418)

GLDS-63: STS-70  
Mammary  
Gland  
(348)

GLDS-21: STS-108  
Skeletal Muscle  
(1303)

GLDS-111: Bion  
Extensor Digitorum  
Longus (66)

GLDS-111: Bion  
Soleus Muscle  
(100)



An increase in aldosterone is associated with metabolic syndrome, which is characterized by chronic inflammation; aldosterone secretion can be triggered by hypoxia.

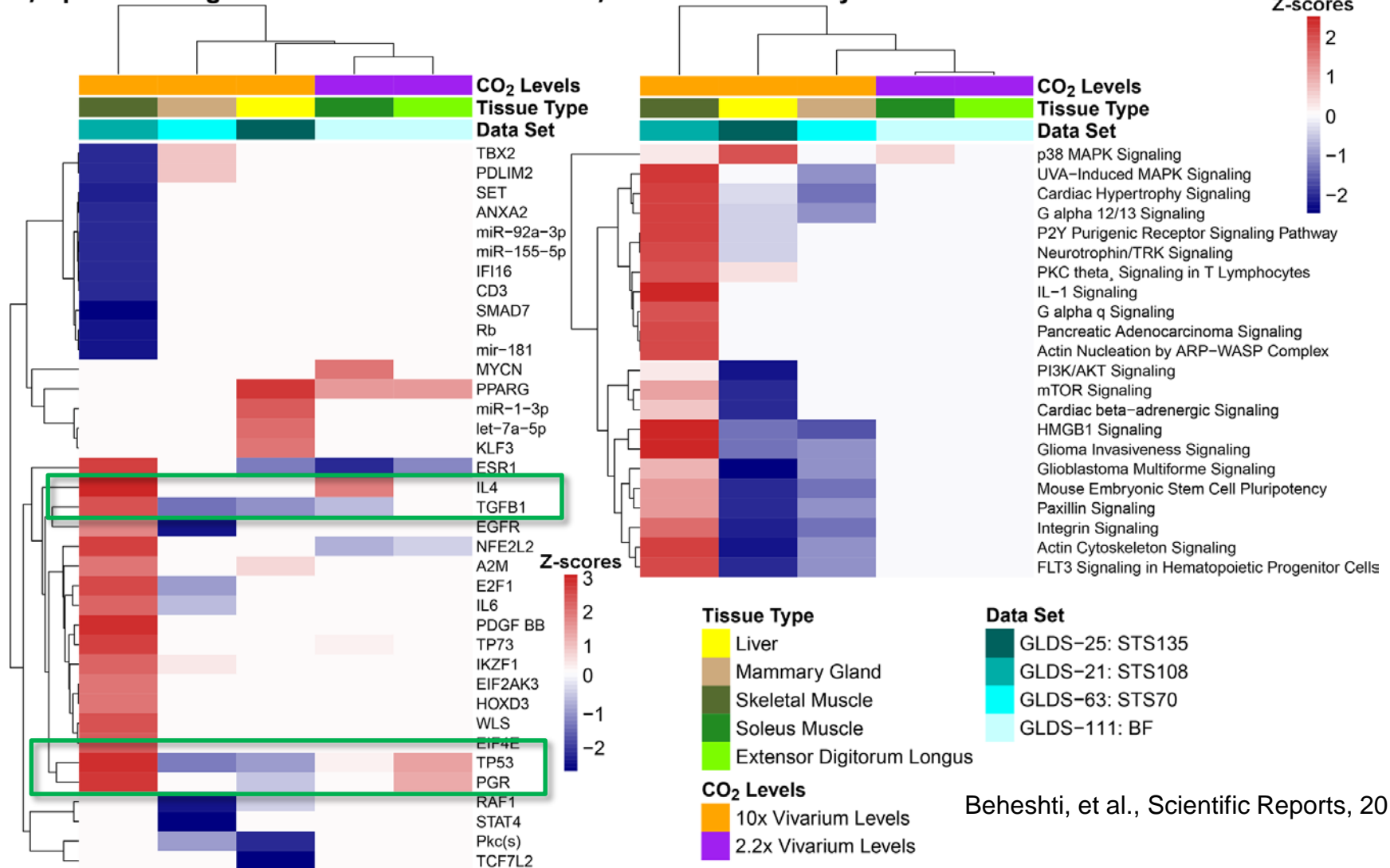


# Upstream regulators and canonical pathways show response is tissue specific and highest for high CO<sub>2</sub>



A) Upstream Regulators: AEM vs Vivarium

B) Canonical Pathways: AEM vs Vivarium



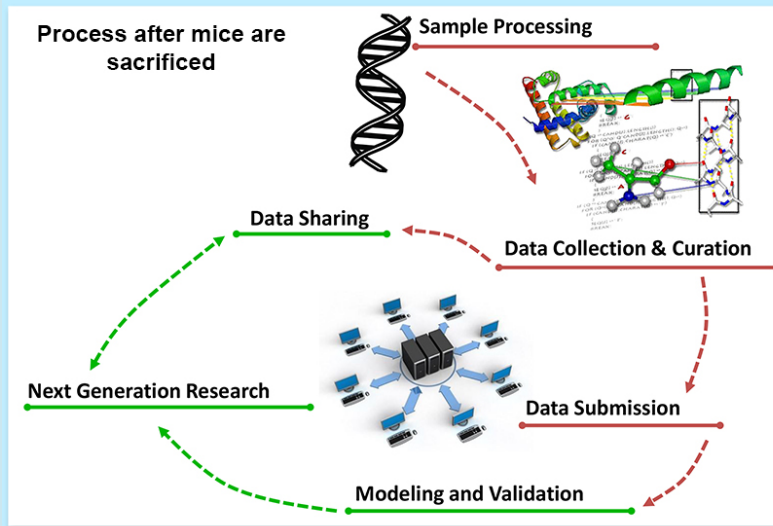
Mild chronic hypoxia due to increased CO<sub>2</sub> levels could explain both the increase in immune responses and a reduction in metabolism – **Need to confirm with AEM experiments at ambient CO<sub>2</sub> levels.**

- Through a systems biology approach we observed global transcriptomic changes in rodents induced by spaceflight-matched environment in AEM cages.
- Identify spaceflight CO<sub>2</sub> levels as a potential environmental stressor that merits experimental investigation
- Systematically changing one environmental aspect at a time (gas concentration, radiation, microgravity, etc.) and analyzing and comparing transcriptional responses could be used to create a network that could predict the most relevant causes and countermeasures for spaceflight-associated conditions, as well as confounding factors for spaceflight experiments.

# **Systems Biology analysis reveals biological spaceflight master regulators**

Beheshti, et al., PLOS One, 2018





Extensor  
Digitorum  
Longus  
Muscle

Soleus  
Muscle

Gastrocnemius  
Muscle

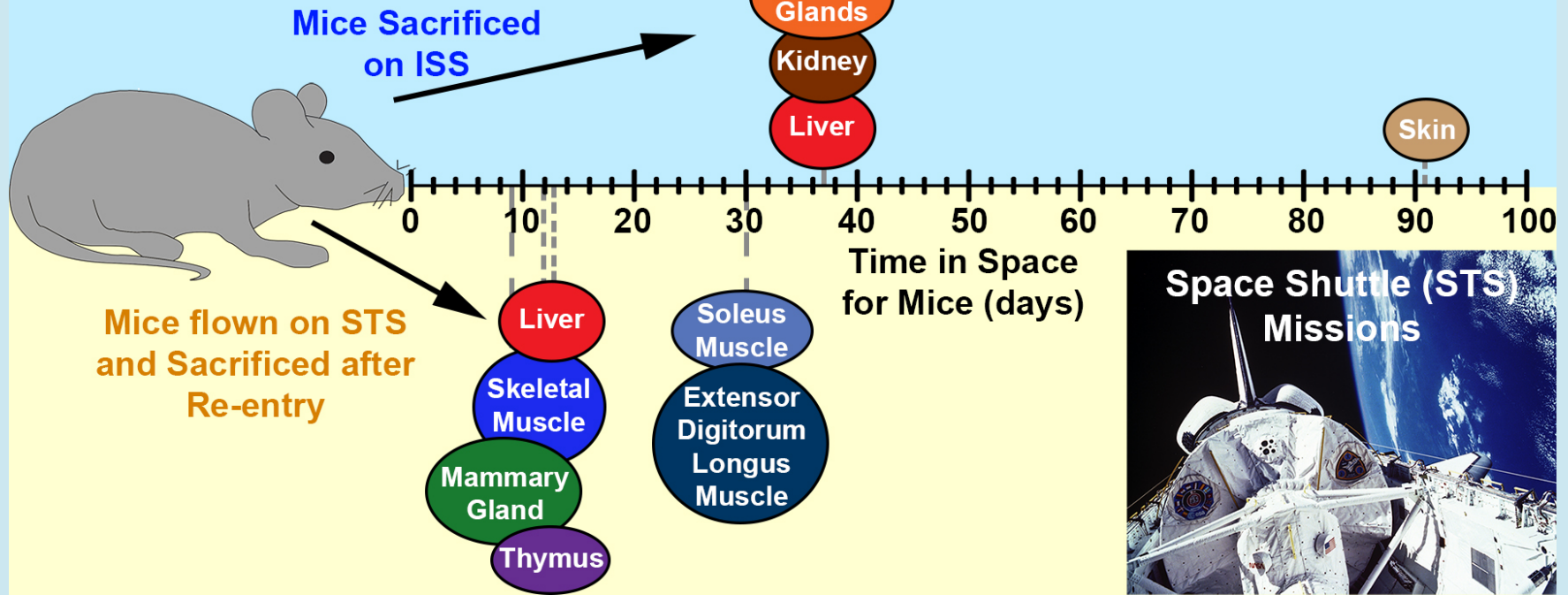
Quadriceps

Tibialis  
Anterior  
Muscle

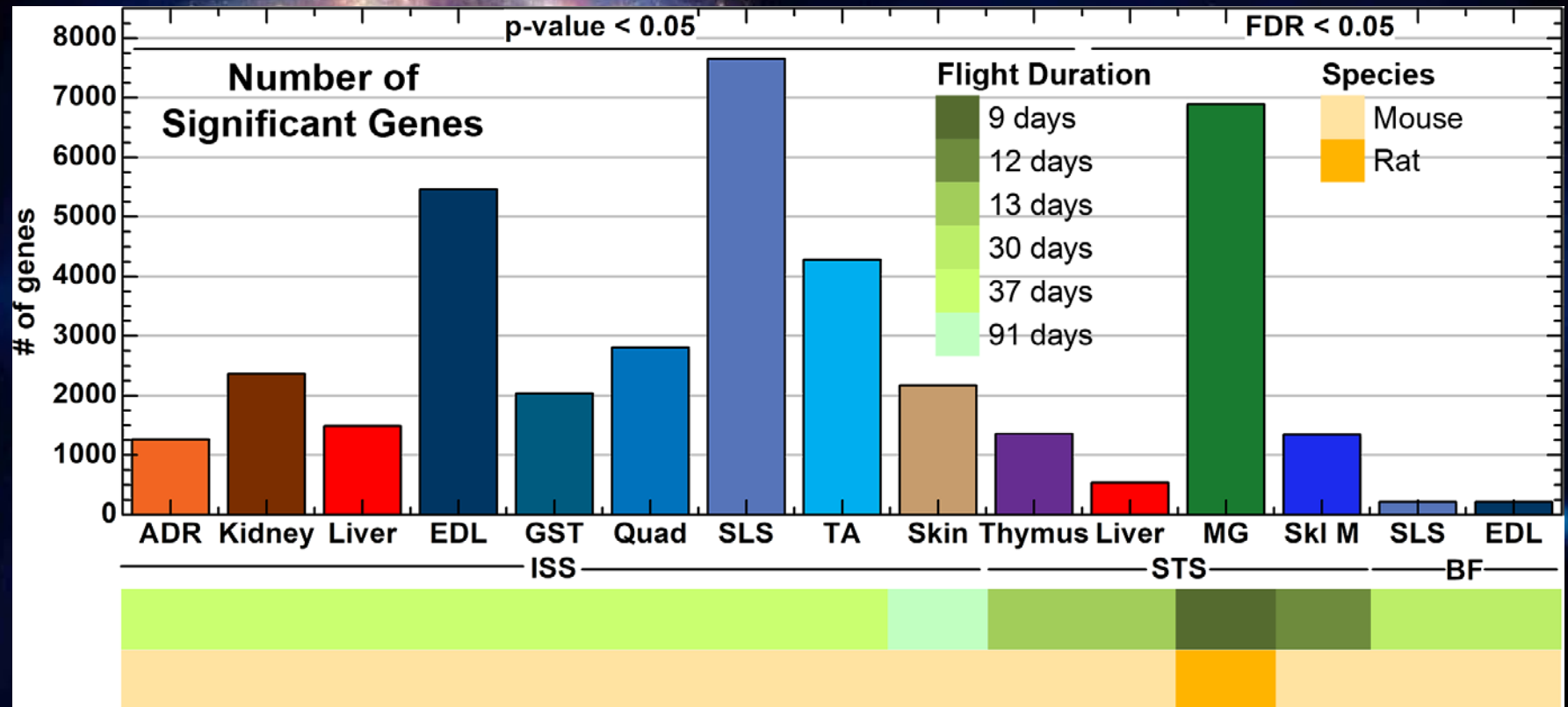
Adrenal  
Glands

Kidney

Liver

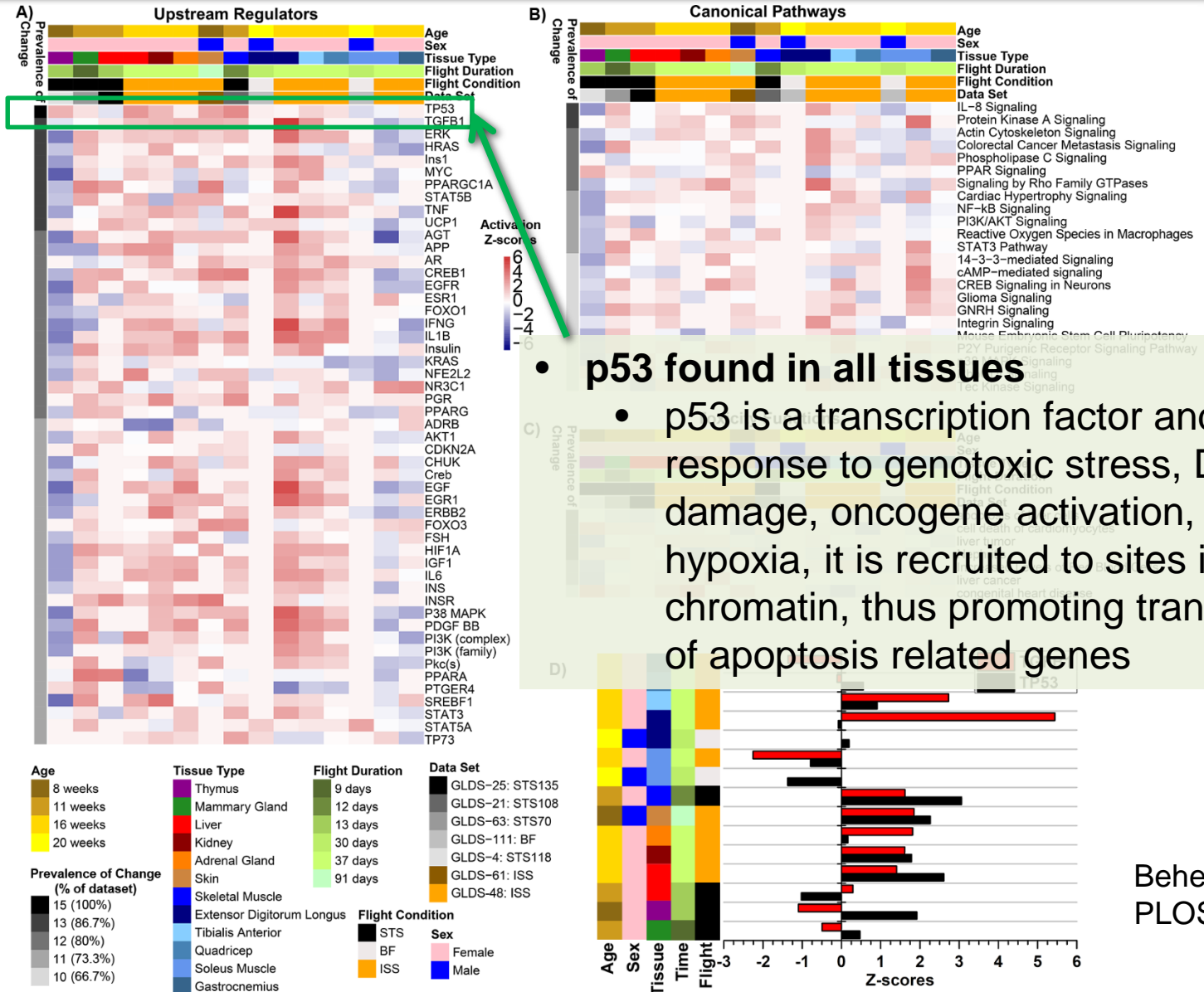


# Number of Significant Genes from Each Dataset



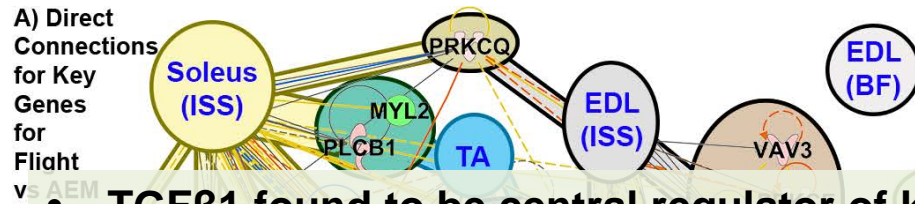
**Fold-Change  $\geq$  |1.2|**

**Pathway/Functional Predictions:**  
Ingenuity Pathway Analysis (IPA)  
Gene Set Enrichment Analysis (GSEA)





A) Direct Connections for Key Genes for Flight vs AEM TO

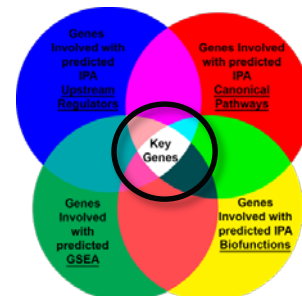


**B) Connections Between all Key Genes for all Datasets (Flight vs AEM):  
Radial Plot with the most Connected Gene in the Middle**



- **TGFβ1 found to be central regulator of key genes**

- TGFβ is known to play a context specific role in sustaining tissue homeostasis predominantly via transcriptional regulation of genes involved in differentiation, cell motility, proliferation, cell survival along with regulating immune responses during homeostasis and infection.
- Previous Studies found reduction in gravitational force to diminish TGF-β expression and apoptosis with higher carcinoembryonic antigen expression in 3D human colorectal carcinoma cells, as compared to 3D cultures in unit gravity.
- In another study, differential regulation of blood vessel growth using basic fibroblast growth factor was identified in modeled microgravity with induction early and late apoptosis, extracellular matrix proteins, endothelin-1 and TGFb1 expression

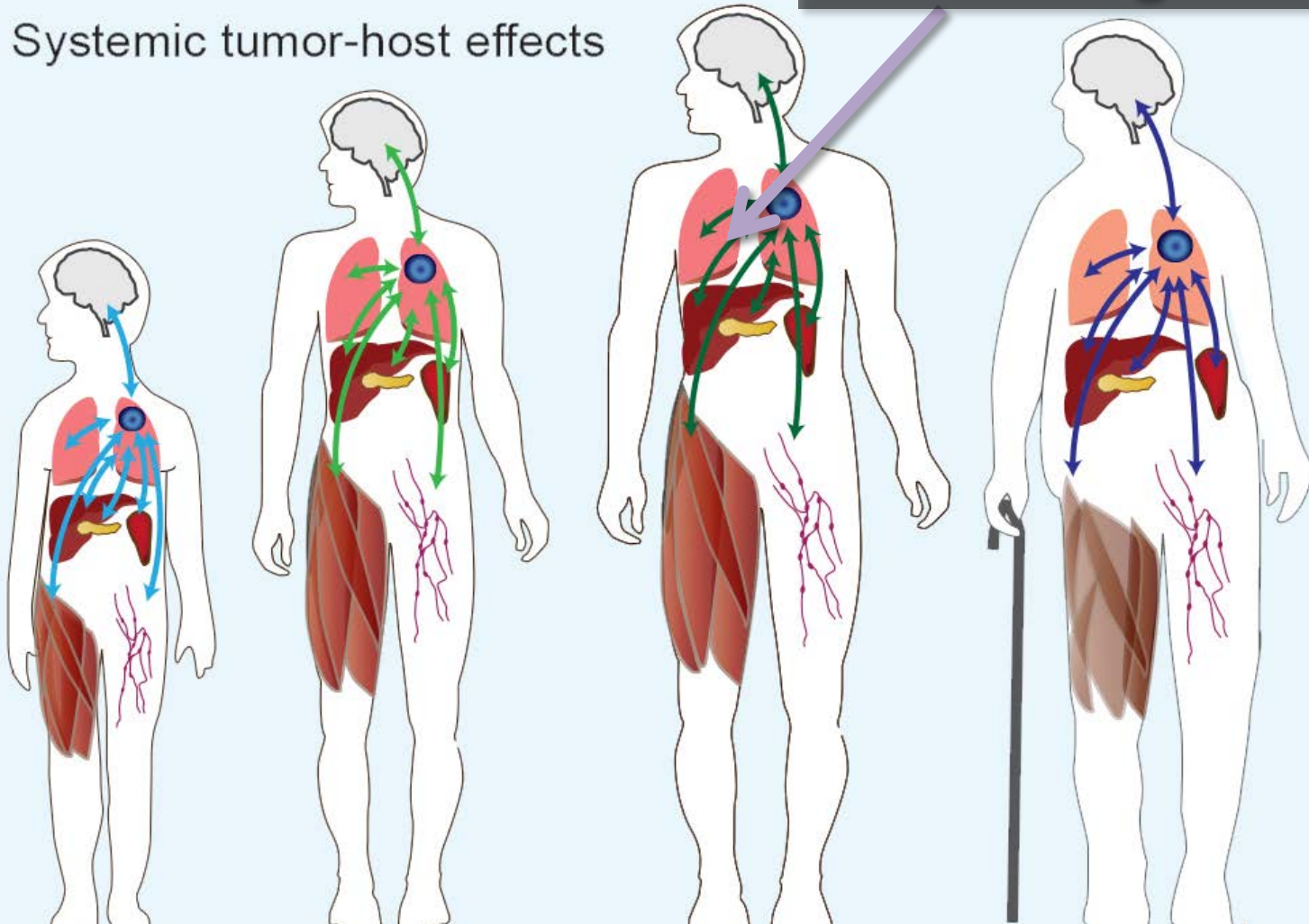




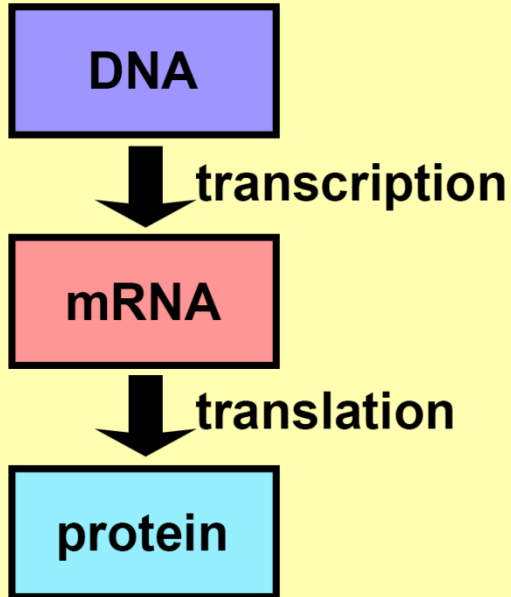
# General Approach to Studying a Systematic Response in the Host

## Circulating miRNAs

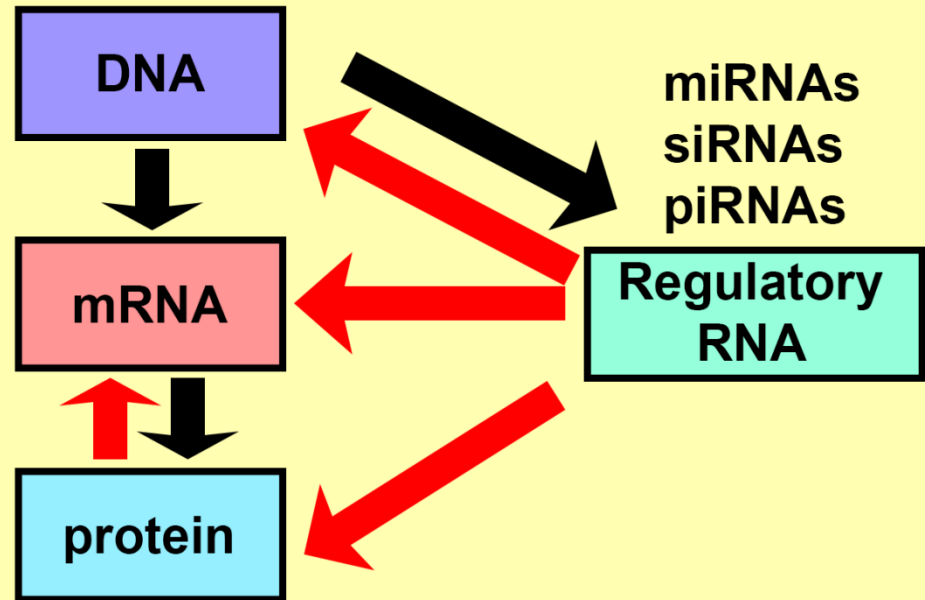
Systemic tumor-host effects



### Classical View of Molecular Biology



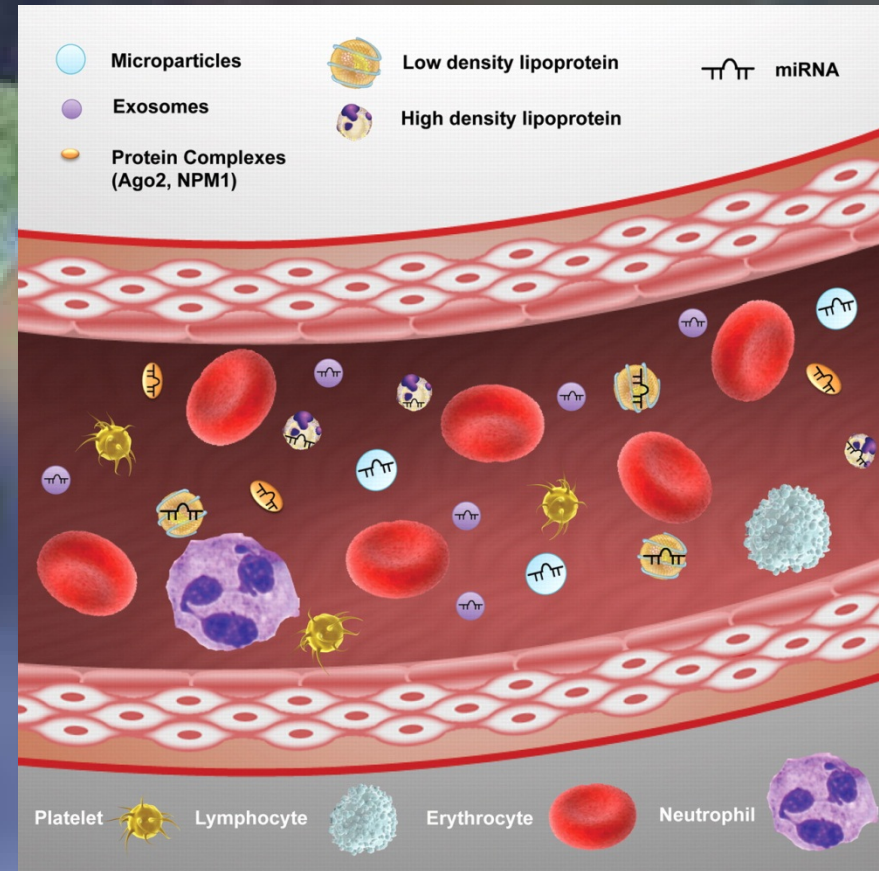
### New Understanding of Molecular Biology



- A single miRNA has been estimated to regulate up to 500 mRNAs
- miRNAs are single-stranded RNA sequences, of about 22 nucleotides in length, processed from longer transcripts.
- miRNAs are important regulators that repress the translation of mRNA transcripts



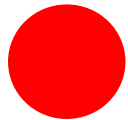
- Circulating miRNAs can carry signals from organs to other various parts of the body through the blood stream.
- The miRNAs can be transported in Exosomes, microparticles, lipoproteins, and outside any type of packaging.
- Our preliminary data shows that a miRNA signature is carried over from the spleen to the tumor with age.
  - Beheshti, et al. *PLoS ONE* 2017



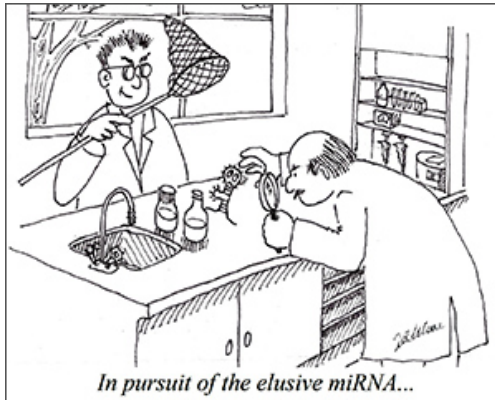
Profiling of circulating microRNAs: from single biomarkers to re-wired networks Anna Zampetaki, Peter Willeit, Ignat Drozdov, Stefan Kiechl, Manuel Mayr. *Cardiovascular Research*, 2011.



**Tumor Suppressor miRNAs**

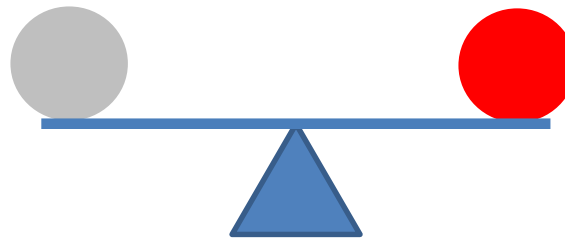


**OncomiRNAs**



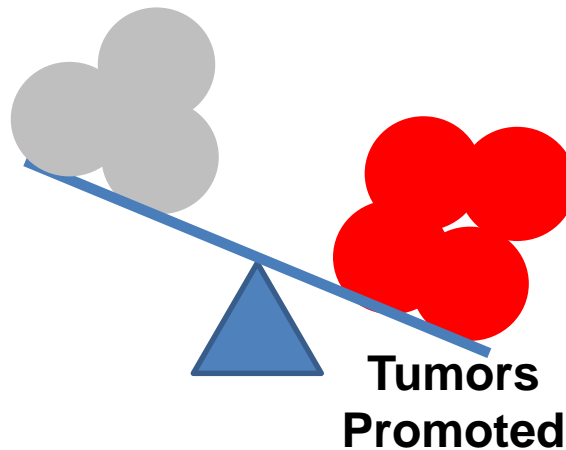
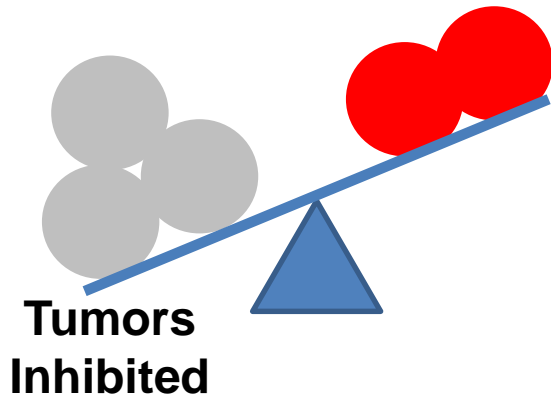
**Tumors  
Inhibited**

**Only looking at a single miRNA**



**No Change in Tumors**

**looking at a pair of miRNAs**



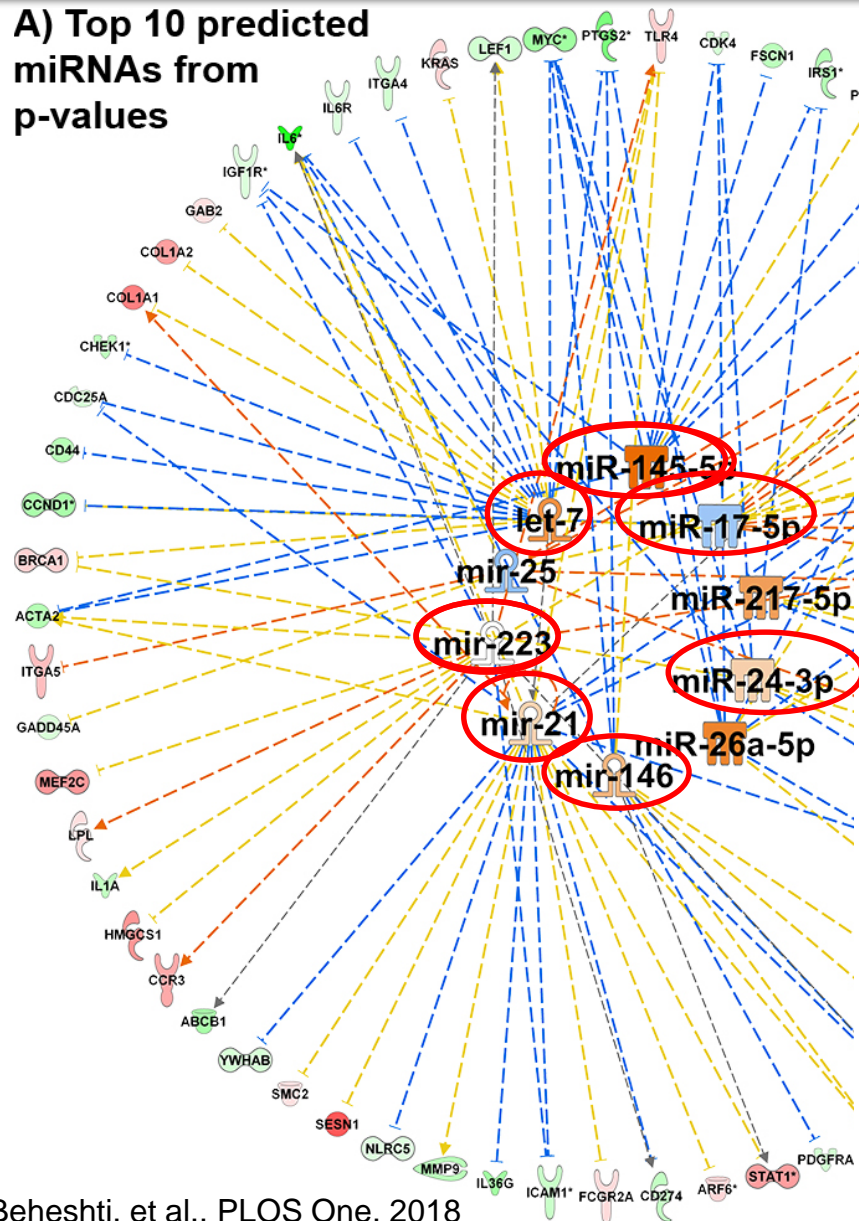
**Systems Biology  
Approach: Looking at  
how the entire system  
impacts the most  
Important miRNAs**



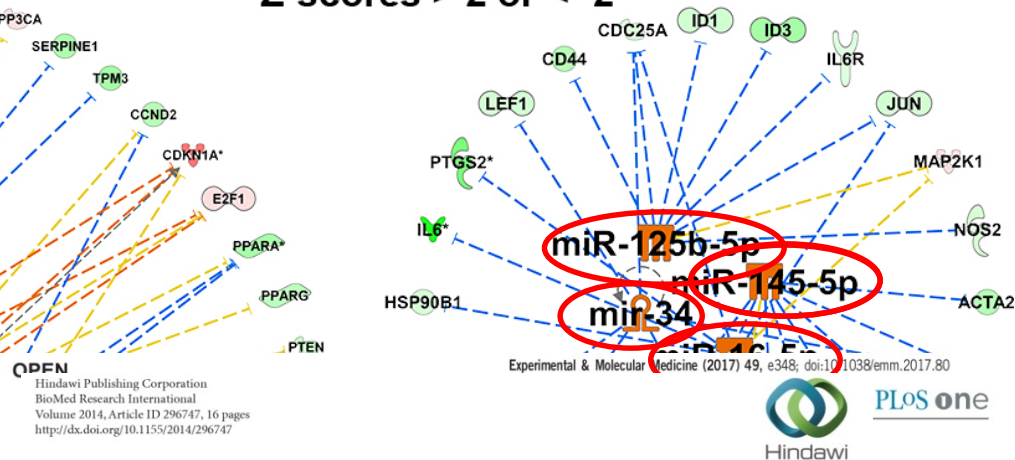
# Predicted miRNAs Involved with Microgravity Effects



## A) Top 10 predicted miRNAs from p-values



## B) All miRNAs with Z-scores > 2 or < -2



OPEN  
Hindawi Publishing Corporation  
BioMed Research International  
Volume 2014, Article ID 296747, 16 pages  
<http://dx.doi.org/10.1155/2014/296747>

Experimental & Molecular Medicine (2017) 49, e348; doi:10.1038/emm.2017.80



## Research Article

### Integration Analysis of MicroRNA and mRNA Expression Profiles in Human Peripheral Blood Lymphocytes Cultured in Modeled Microgravity

C. Girardi,<sup>1</sup> C. De Pittà,<sup>1</sup> S. Casara,<sup>1</sup> E. Calura,<sup>1</sup> C. Romualdi,<sup>1</sup> L. Celotti,<sup>1,2</sup> and M. Mognato<sup>1</sup>

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Received 16 April 2014; Revised 22 May 2014; Accepted 22 May 2014; Published 23 June 2014

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We analyzed miRNA and mRNA expression profiles in human peripheral blood lymphocytes (PBLs) incubated in microgravity condition, simulated by a ground-based rotating wall vessel (RWV) bioreactor. Our results show that 42 miRNAs were differentially expressed in MMG-incubated PBLs compared with 1 g incubated ones. Among these, miR-9-5p, miR-9-3p, miR-155-5p, miR-150-3p, and miR-378-3p were the most dysregulated. To improve the detection of functional miRNA-mRNA pairs, we performed gene expression profiles on the same samples assayed for miRNA profiling and we integrated miRNA and mRNA expression data. The functional classification of miRNA-correlated genes evidenced significant enrichment in the biological processes of immune/inflammatory response, signal transduction, regulation of response to stress, regulation of programmed cell death, and regulation of cell proliferation. We identified the correlation of miR-9-3p, miR-155-5p, miR-150-3p, and miR-378-3p expression with that of genes involved in immune/inflammatory response (e.g., IFNG and IL17F), apoptosis (e.g., PDCD4 and PTEN), and cell proliferation (e.g., NKX3-1 and GADD45A). Experimental assays of cell viability and apoptosis induction validated the results obtained by bioinformatics analyses demonstrating that in human PBLs the exposure to reduced gravitational force increases the frequency of apoptosis and decreases cell proliferation.

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# Predicted miRNAs Involved with Microgravity Effects



## Health Risk Due to miRNAs



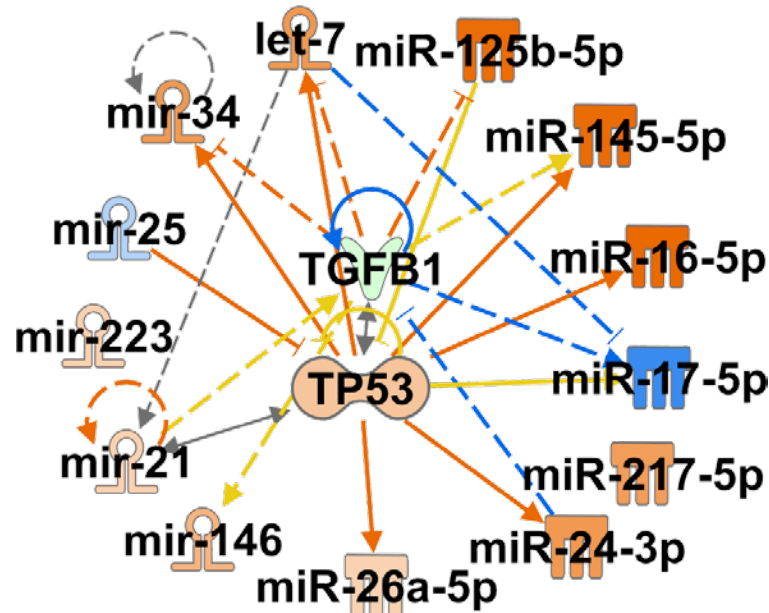
○ Predicted Activation

○ Predicted Inhibition

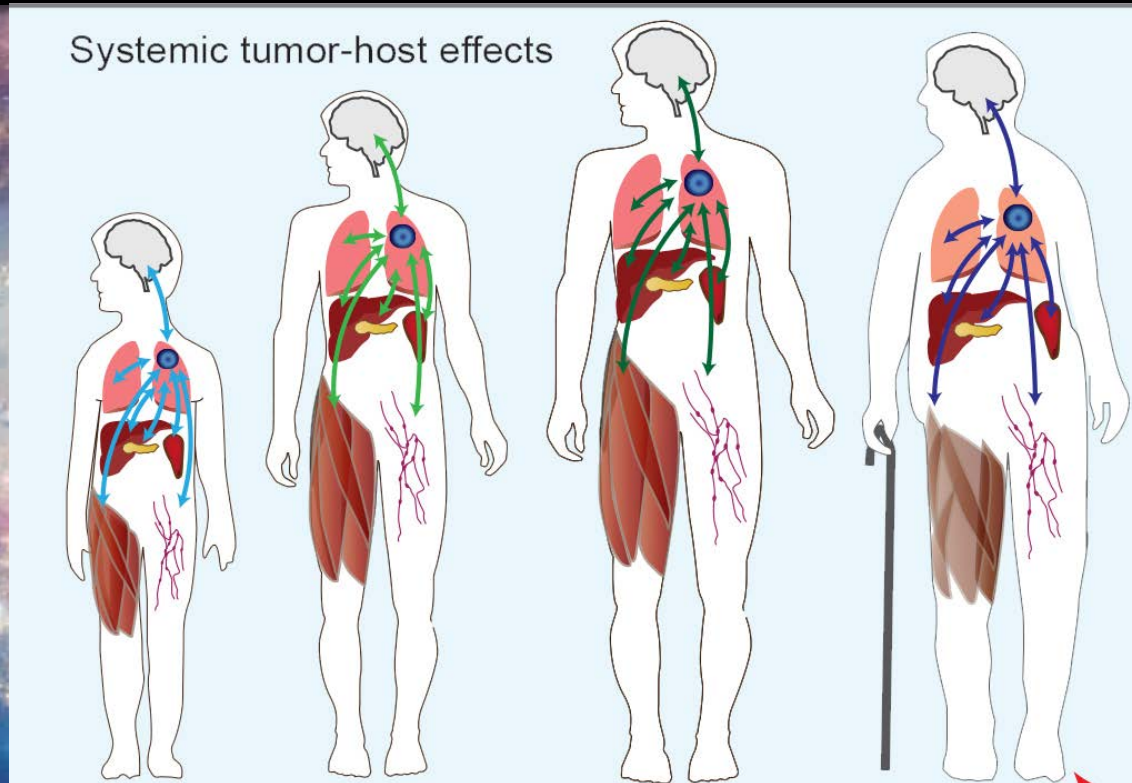
○ Negative Impact on Health

- A recent report showed that inactivation of p53 altered TGF- $\beta$  signaling, which ironically displayed both tumor-suppressive and pro-oncogenic functions. p53 functions to integrate crosstalk between Ras/MAPK and TGF- $\beta$  signaling via binding to Smad3, dislocating the Smad3/Smad4 complex formation and differentially regulating subsets of TGF- $\beta$  target genes

*Biological Health  
Risk Increased*







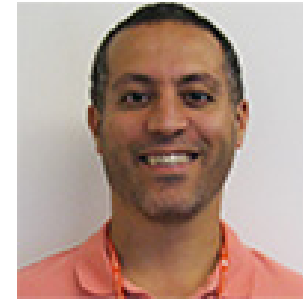
- **Systems biology approach allows for systemic understanding of the impact of Microgravity.**
- **Circulating miRNAs can influence overall progression of health risk to the host.**
- **miRNAs can potentially be used for novel minimally invasive therapeutics and countermeasures**
- **GeneLab ([genelab.nasa.gov](http://genelab.nasa.gov)) is a powerful tool to generate hypotheses and direct future space research**

# **Analysis Working Group (AWG) Member related work determines novel systemic biological factors causing damage due to spaceflight**

Work in progress



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UNIVERSITY of CALIFORNIA, SAN DIEGO  
SCHOOL OF MEDICINE

Deanne Taylor    Hossein Fazelinia    Komal Rathi

Children's Hospital  
of Philadelphia™Perelman  
School of Medicine  
UNIVERSITY of PENNSYLVANIA

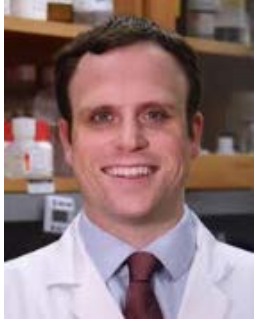
Helio Costa    Kathryn Grabek

STANFORD  
UNIVERSITYHAMPTON  
UNIVERSITY  
THE STANDARD OF EXCELLENCE

Gary Hardiman    Willian da Silveira

MUSC Health  
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Chris Mason



Cem Meydan



Jonathan Foox



Flavia Rius



Cornell University



Yared Kidane

TEXAS  
SCOTTISH RITE HOSPITAL  
FOR CHILDREN

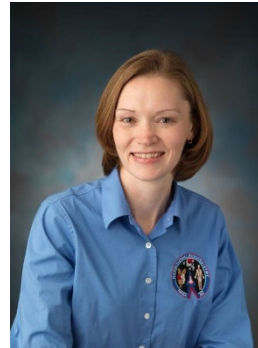
Susana Zanello



Scott Smith



Manned Space Flight Education Foundation



Sara Zwart



Afshin Beheshti



Sylvain Costes

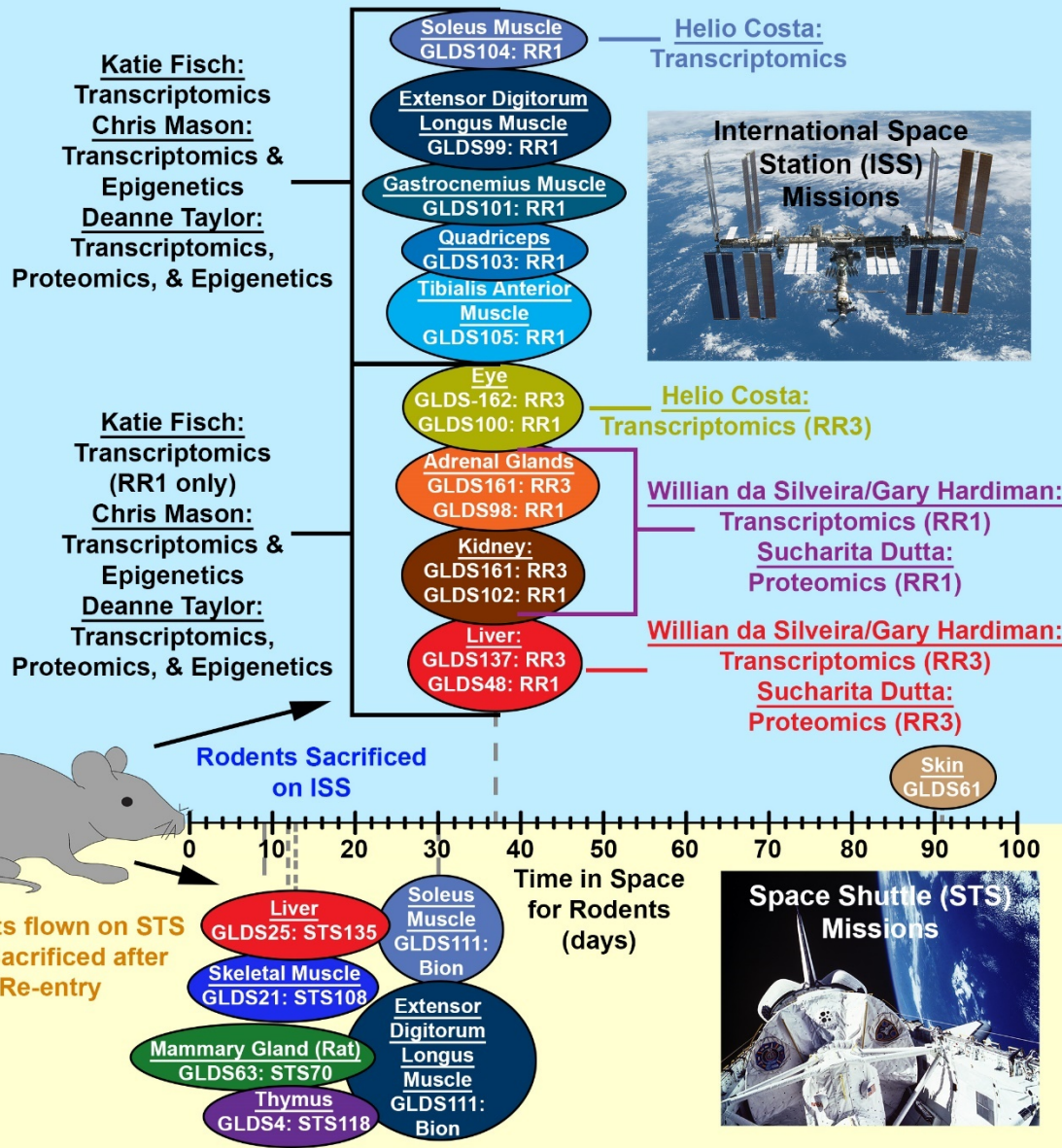




# Specific Datasets and Tissues AWG Members Analyzed



- Additional Datasets that are being analyzed:
  - Human datasets
    - GLDS-54, GLDS-174, GLDS-86, GLDS-118, GLDS-53, GLDS-54, GLDS-13, GLDS-52, or GLDS-114 (Tyson McDonald and Yared Kidane)

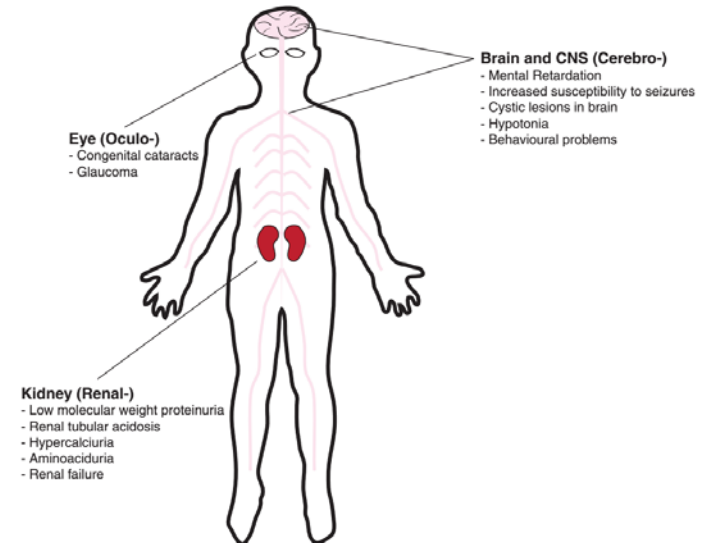


# Hypothesis Developed and Being Worked On



- Spaceflight changes the physical properties of the cell components impacting from the molecular to the whole body level.
- The Mitochondria are the principal cellular component affect.
- The Liver is the principal organ affected in issues related to the metabolism.
- Possible disease that can be associated with liver damage and pathways is: Oculocerebrorenal Syndrome of Lowe
  - “Extensive research has demonstrated that OCRL-1 is involved in multiple intracellular processes involving endocytic trafficking and actin skeleton dynamics. This explains the multi-organ manifestations of the disease.”
  - “The classic form of the oculocerebrorenal syndrome of Lowe (OMIM #309000), first described by Lowe et al. in 1952 [1], is characterized by the triad of congenital cataracts, severe intellectual impairment, and renal tubular dysfunction with slowly progressive renal failure”
  - Patients with this disease manifest Cataract, Glaucoma and Muscle hypotonia.

Schematic diagram showing the organs affected in Lowe syndrome



Mehta, Zenobia B et al. “The Cellular and Physiological Functions of the Lowe Syndrome Protein OCRL1.” *Traffic* (2014).

<https://genelab.nasa.gov>

## Participate in GeneLab Analysis Working Groups

- Social media :
  - @NASA Ames **Facebook**
  - **Twitter** #GeneLab
  - **ResearchGate**: <https://www.researchgate.net/project/Omics-for-Space-Biology-The-GeneLab-project>



Chris Barreras  
**Afshin Beheshti**  
**Dan Berrios**  
**Valery Boyko**  
Sonja Caldwell  
Jairon Camarillo  
Egle Cekanaviciute  
John Costa  
**Sylvain Costes (PM)**  
Marie Dinh  
Sandy Dueck  
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Dennis Heher  
Lynn Hutchison  
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Tristan Le  
Qiang Li  
Shu-Chun Lin  
Sneha Raghunandan  
Shayoni Ray  
**Sigrid Reinsch**  
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